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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 11 1953

A MECHANICAL HEART-LUNG FOR USE IN MAN

BY

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With a Foreword by IAN AIRD, Ch.M., F.R.C.S.

Professor of Surgery, Postgraduate Medical School of London

Foreword

Some years ago the department of surgery in the Postgraduate Medical School of London was concerned with research in the perfusion of isolated human organs. The perfusion of isolated organs by blood artificially oxygenated and propelled by a mechanical pump cannot be continued for more than a few hours. After some hours the perfused organ swells visibly and the outflow of blood from it progressively and rapidly diminishes. After a short and not very successful examination of the problem of prolongation of the survival time of isolated organs in these conditions attention was turned to the extracorporeal heart–lung circulation for the maintenance of the circulation of the experimental animal by a total replacement of its own heart and lungs, comparable to that which would be required in the application of an apparatus of this kind to intracardiac surgery. It seemed to us, after some experience in this field, that a machine to undertake the whole function of heart and lungs in a patient subjected to intracardiac surgery was not yet an immediately attainable aim.

Animals maintained entirely on an extracorporeal heart–lung circulation sometimes survive for indefinite periods, but a high proportion fail to survive, perhaps for reasons not dissimilar to those which make prolonged perfusion of the isolated organ impossible. The natural lung may have other functions than oxygenation. In any case, there are immediate practical difficulties in employing a heart–lung machine to replace the heart and lungs of a patient subjected to cardiac surgery. Heparinization must be complete, and the difficulty of obtaining a bloodless field even in a heart to which blood is not returned by the venae cavae has already been demonstrated at least once in man. Our attention accordingly passed to the use of a heart–lung machine as a form of "assisted circulation."

Our aim in this field became the ultimate use of an artificial heart–lung machine for the treatment of certain acute forms of cardiac or pulmonary failure. The value of artificial oxygenation of the blood for even a short period in acute pulmonary oedema or status asthmaticus seemed obvious enough, for, provided the patient can be kept oxygenated for a time, these pathological circumstances are often self-limiting. In coronary thrombosis there are patients in whom it might be expected that the temporary provision of a high aortic pressure might tide the patient over a fatal low-pressure period, and might improve such coronary circulation as was still open. In congestive heart failure, when failure has been due to a relatively small fall in a previously low cardiac output, to withdraw blood from the congested veins and to perfuse it oxygenated into an arterial tree would seem to combine the advantages of venesection and adequate oxygenation. The mechanism would have a particular advantage in preparing grossly cyanotic sufferers from mitral stenosis for a valvulotomy which they could not otherwise sustain. Dr. Melrose proceeded to devise an apparatus which might ultimately be applied to these and similar purposes and to test that apparatus in the form of an assisted circulation in parallel with the natural circulation of an experimental animal. The results of his whole-time activity in this field over a period of four years are recorded in the two papers which follow. His data indicate that his machine might now be justifiably and humanely applied to certain varieties of anoxia and circulatory failure in man.

*Part of the work was done under the tenure of a Studentship in Research from the Medical Research Council.

Artificial Maintenance of Life

The possibility of maintaining life artificially in animals or parts of animals has excited the interest of many over the last century. Numerous attempts have been made to create an apparatus capable of this, but until the last decade these efforts have been sporadic and isolated in character. The publication by J. H. Gibbon, jun., in 1937 of a paper on artificial maintenance of the circulation during experimental occlusion of the pulmonary artery heralded the beginning of a new approach to the problem. His object was to short-circuit the heart and lungs of animals to allow intracardiac surgery in a bloodless field. Coinciding as it did with the emergence of a new era in surgery—that of replacement rather than ablation—his work stimulated a great new interest and challenge which was taken up in many surgical centres. This challenging problem was, and still remains, to produce an extracorporeal apparatus capable of maintaining temporarily the entire circulation of the human body.

Contributions in this field from Crafoord and Björk in Sweden, Kolff and Jongbloed in Holland, André Thomas in France, Dennis and Leland Clark in America, and many others have resulted in continuous progress, and now the stage is almost set for clinical use.

Stimulated by these advances, it was decided in 1949 that a machine should be constructed to serve three purposes. First, to carry temporarily a part of the cardio-respiratory function when the function of either or both of these organs is impaired ; secondly, to provide a complete diversion of the blood stream away from the chambers of the heart in order to permit intracardiac surgery ; and, thirdly, to perfuse isolated organs.

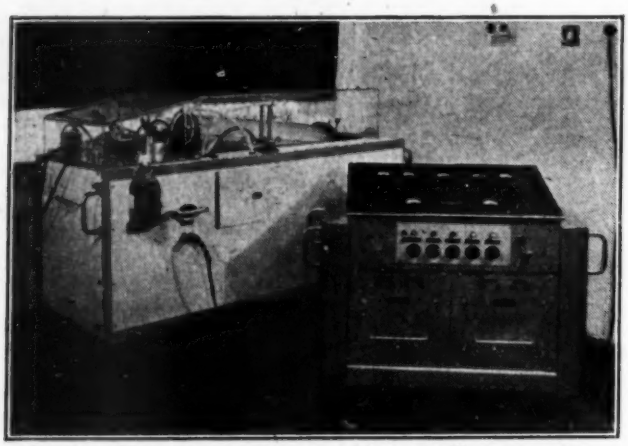

FIG. 1.—The pump-oxygenator with controlling apparatus.

The Pump-oxygenator

Initially, considerable experience was gained with a pump-oxygenator essentially similar to that described by Björk (1948a) and Crafoord (1949). In this machine a number of disks dip into a trough of blood ; when rotated they pick up on their surfaces thin films of blood, exposing them to an atmosphere of oxygen, and in this way create a large gas–liquid interface. After this method had been investigated and compared with other methods, particularly those involving the dispersal of oxygen as minute bubbles, it was decided to embody the principle of rotating disks in a machine of novel design capable of circulating adequately oxygenated blood at a rate of at least 3 litres a minute (Fig. 1).

Two factors are important in the utilization of this principle. The first is that the optimum period for which each red blood cell should be exposed to oxygen is in the region of half a second. The second factor is that the exposure time must be achieved without increasing above a definite maximum the speed of rotation of the disks. Rotational speeds in excess of 80 r.p.m., corresponding to a velocity at the periphery of the disks of 52 cm. a second, frequently lead to foaming of the blood.

These two factors are of major importance, since they limit the effective area for oxygenation of each plate, but there are others which also affect the efficiency of such machines. These are : (1) The area of interface between blood and gas should not vary with changes in the volume of blood in the machine. (2) Mixing of blood should be very complete, for no provision can be made to replace completely each saturated film, after exposure to oxygen, with one as yet unsaturated. (3) The measures to ensure mixing should not impede smooth and rapid flow through the machine. (4) Foaming if it occurs should not greatly interfere with the efficient operation of the artificial lung. (5) The apparatus should be capable of being completely dismantled for effective cleaning. (6) Adequate surface area should be obtained without the use of a very large volume of blood to charge the machine. (7) For ease in maintaining sterility, a system as nearly closed as possible is desirable.

From these considerations it is seen that enlarging the diameter of the disks makes a longer exposure of time inevitable if a safe rotational speed is to be maintained, while increasing the number of disks greatly increases the blood volume required for charging. Neither of these measures, nor a combination of them, confers any improvement in the mixing, or in ensuring the maintenance of an optimum blood film size.

The Oxygenator

The new oxygenator (Fig. 2) is essentially a rotating cylinder set at a slight angle to the horizontal. Within it blood travels under the influence of gravity from one end to the other, and is spread over a multitude of surfaces formed by blades projecting into the lumen of the cylinder. These blades are arranged within the cylinder somewhat in the form of an Archimedean helix. This analogy is not strictly accurate, but may clarify the method of construction, which is in fact carried out in the following manner. A cylinder of "perspex" 30 in. (76 cm.) in length and of internal diameter of 8 in. (20.3 cm.) is free to rotate in its long axis while supported on rollers at 20 degrees to the horizontal. It is closed at each end by an end-plate of "tufnol" 10 in. (25.4 cm.) in diameter. In this cylinder

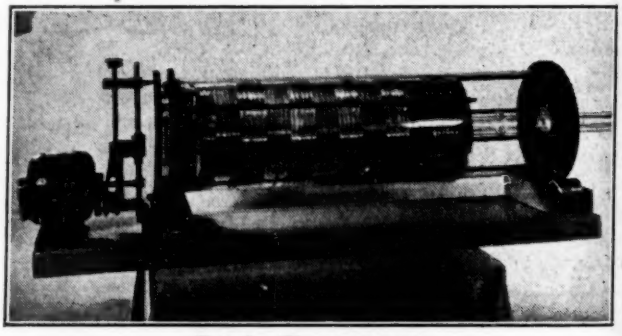

FIG. 2.—The oxygenator.

annular plates of 1/24 in. (1 mm.) perspex, with an overall diameter of 7¾ in. (20 cm.) and an internal diameter of 4¾ in. (11 cm.), are separated one from the other by annular washers. These washers have the same external diameter as the plates but an internal diameter of 5⅜ in. (13.6 cm.).

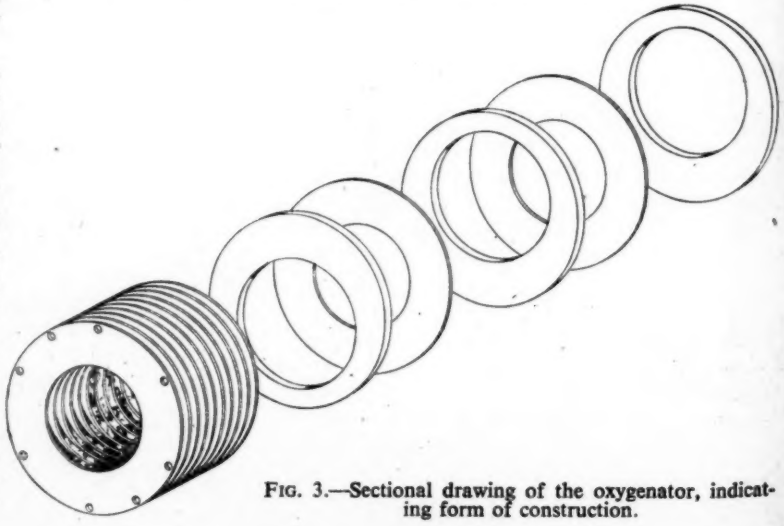

FIG. 3.—Sectional drawing of the oxygenator, indicating form of construction.

They are constructed from perspex 5/16 in. (0.8 cm.) thick. The holes in the plates are concentric, but the holes in the washers are cut eccentrically, the centres of the hole being 1 in. (2.54 cm.) from the true centre of the washers.

These plates and washers are mounted in the cylinder on chromium-plated rods and are freely detachable for cleaning. A maximum of 76 plates and their separating washers may be used to provide a surface area of approximately 1 square metre.

The plates (Fig. 3) are fitted so that their central holes form a cylindrical cavity, coaxial with the enclosing cylinder, but the arrangement of the washers between each plate varies with each group of five. Each group of five washers are mounted so that the holes in them form a cylinder eccentric to the cylinder formed by the holes in the plates, and, as the internal diameter of the washers is larger by 1 in. (2.54 cm.) than that of the plates, these plates project as crescents within the cavity formed by the holes in the washers. Each group of five washers and plates is arranged relative to the next group so that crescentic protrusions of the plates are at opposite poles. In sagittal section, therefore, the cylinder presents a series of alternating platforms and troughs, these troughs being subdivided into five compartments by the five plates (Fig. 4).

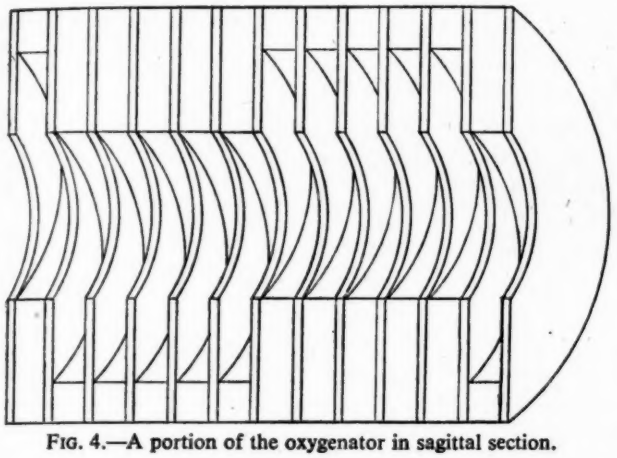

FIG. 4.—A portion of the oxygenator in sagittal section.

Passage of the Blood

In describing the path of the blood passing by gravity along the tilted oxygenator, it is helpful to consider first the hypothetical case in which both washers and plates are fitted so that the holes in them are concentric. A pool of blood would lie along the base of the cylinder formed by the holes in the washers to the depth of the level of the holes in the plates. Rotation of the oxygenator would not affect the position of the pool in space. Where the holes in the washers are eccentric to the holes in the plates and the circumferences of these holes touch at one point in any group of five, a different action is apparent. When the point of touching is at top centre a pool of blood will be formed as in the previous case. During any revolution, as the point of touching approaches bottom centre this pool will be emptied by the action of the washers, which in effect rise to the level of the holes in the plates. The alternation of phase between adjacent groups ensures that as a pool in one group empties so it is re-created in the next group.

Further, during any revolution the crescentic projections of the plates are alternately fully covered by the pool of blood, and also, together with adherent films of blood, fully exposed to the gas contained in the oxygenator.

The stream of blood passing down the oxygenator is alternately raised and lowered by the action of the washers. This action avoids the necessity of the edges of the plates cutting across the streamline in order that they may become covered with blood. In fact, blood is poured over the plates and into the pool formed between them, then raised up and carried down the oxygenator before being poured over the succeeding group of plates.

This arrangement permits a thorough mixing of the blood with a smooth and rapid passage along the machine. It also ensures that all the available surface area is utilized without reference to the volume of blood contained in the machine. Furthermore, it enables the machine to work with a relatively small charge of blood.

The cylinder is rotated by a friction wheel, driven by an electric motor. Adjustment of the position of the driving wheel in relation to the diameter of the end-plate allows cylinder speeds between 24 and 120 revolutions a minute to be obtained. At maximum speed the surface area exposed per minute is in the region of 120 square metres, though it is preferable to use only as great a rotational speed as is necessary to obtain efficient oxygenation.

The inlet and outlet tubes for the blood, together with the inlet for oxygen and a fourth tube used to estimate the level of the blood in the collecting chamber, enter at one end. These tubes are carried by a perspex rod which passes through a simple felt seal in one end-plate down the centre line of the oxygenator to a chronium-plated bearing on the other end-plate. No attempt has been made to make a gas-tight seal, though this is undoubtedly possible.

Experience has shown that the distance between the plates can be reduced from 5/16 to 3/16 in. (0.8 to 0.48 cm.) without increasing the danger of foaming. It is expected that a moulding in nylon or teflon (polytetrafluorethylene) will be produced combining both washer and plate, and this will enable the number of parts to be halved. It will also enable autoclaving to be used for sterilization. This latter point is undoubtedly of great importance, and might be considered essential in a machine for use in human beings. Further, during the moulding process a large number of corrugations can be pressed into the surface of the plates and the surface area of each greatly increased.

The Pumping Circuit

Since the oxygenator is not part of a closed circuit, it is essential that two pumps be used; one to act as the right side of the heart to supply the artificial lung and the other as the left side of the heart to return oxygenated blood to the recipient.

The pumping circuit must not only be capable of circulating blood at physiological rates and pressures without destroying its constituents, but must also be capable of exact regulation. For this purpose the most satisfactory pump is a rotary type without valves in which an elastic tube, through which the blood passes, is squeezed within the pump by the action of a roller. The decision to employ this type of pump was made after comparison with many forms of the Dale–Schuster pump. It has obvious advantages over the latter in simplicity and ease of sterilization, but had a disadvantage in that the action of the roller in squeezing the tube sometimes caused greater haemolysis. Investigation revealed that this was largely due to the scrubbing of one wall of the tube on the other, an effect produced by the severe shearing forces set up by the roller in squeezing the tube. Re-design of the pump tested, a model based on the design of Henry and Jouvelet, resulted in a considerable reduction of this effect, which in turn reduced the rate of haemolysis by as much as 70% in some comparisons.

The pump (Figs. 5, 6, 7, and 8) now used consists of a circular housing in which there is clamped a loop of tube. Within this loop is a large single roller free to rotate on ball-bearings which are mounted on a compound driving shaft. This shaft is made up in the following way. A central driving spindle has fixed to it a cam, the centre of which is ¼ in. (0.6 cm.) from the true centre. On this cam is carried an outer cam the centre of which is also ¼ in.

from the true centre. This outer cam is free to rotate about the inner one, but may be locked in any position. Adjustment of the outer cam on the inner one provides any degree of throw from 0 to ¼ in. (1.3 cm.). In operation the outer cam is adjusted so that the roller carried on the shaft just closes the lumen of the tube in the pump. Then rotation of the driving spindle carries the roller around the inner wall of the pump housing, causing it to squeeze the tube in such a manner that a pumping action is obtained. Adjustment is simple and rapid, no blood comes into direct contact with any moving parts, and a pulsatile flow is obtained.

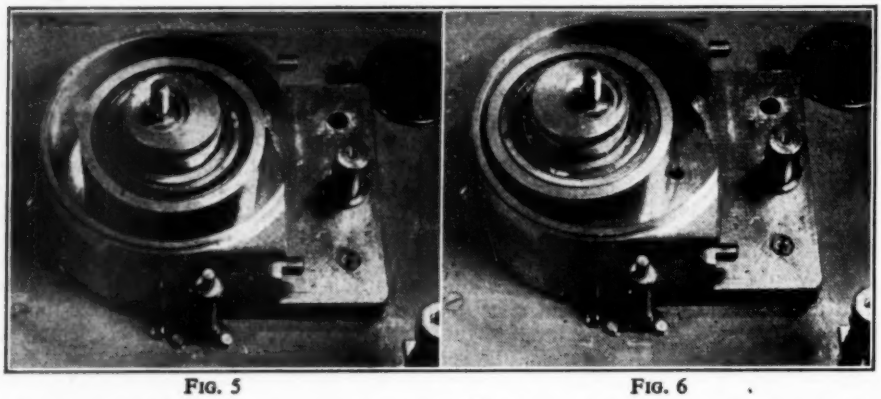

FIG. 5 FIG. 6

FIG. 5.—One of the pumps unassembled, with the roller in a concentric position within the circular housing. FIG. 6.—The roller moved to a fully eccentric position.

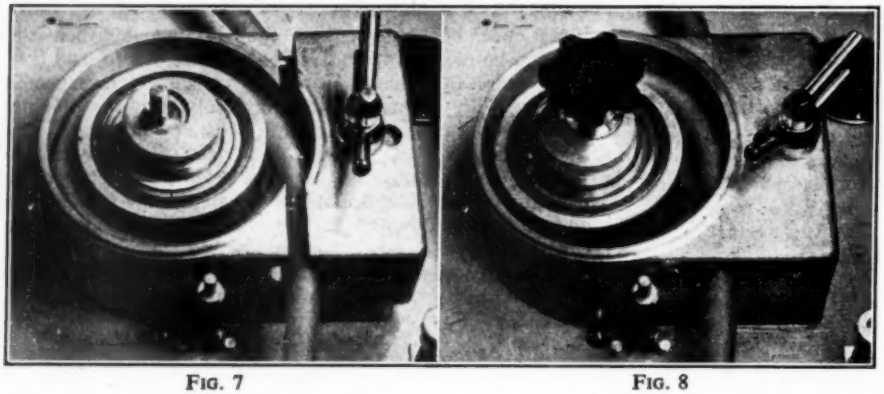

FIG. 7 FIG. 8

FIG. 7.—A loop of tubing in position between the pump housing and the roller, which is in the concentric position. FIG. 8.—The pump fully assembled. The tube is clamped within the pump housing and is compressed by the roller, which has been adjusted to a degree of eccentricity sufficient to close the lumen of the tube.

Control Mechanism

The stroke volume depends only on the bore of the tube, and in the pump used this may be varied from ¼ to ½ in. (0.3 to 1.3 cm.) Both pumps are driven by fractional horse-power D.C. shunt wound motors through reduction gearing and belt drive. These motors are of special type and are so designed that their speed may be controlled over a 10: 1 range by magnetic amplifiers (English Electric ¼ h.p. "magamp"). These amplifiers have no thermionic valves in them and are almost mechanical in operation, gaining thereby in reliability and stability. They can be controlled by hand, and such adjustment will enable the circulation to be operated under direct control. However, a rather more sensitive control is achieved by an electronic apparatus designed to replace the delicate balancing mechanism of the animal. This control gear takes as its guide three quantities measured continuously by electrical manometers. These are of the differential-transformer type and are particularly stable. One measures the volume of blood in the artificial circuit from the depth of blood in the collecting chamber of the oxygenator, one measures the pressure at which the arterial pump is working, and one measures the pressure at which the venous pump is working. The signals from the three manometers are used to form a pattern of servo-loops which result in automatic adjustment of the pumping speed.

The most important function of the control is to ensure that the volume of blood in the machine is constant within narrow limits under varying conditions. As no two pumps of the type employed can be relied upon to deliver constantly matched outputs, it is essential that the rates should be controlled from the blood volume within the artificial circulation, as this will give a true indication of any imbalance between the two. For this reason the signal from the volume indicator manometer is used to induce the two pumps to work at such speeds that they will deliver the same blood flow.

The signal derived from the arterial pressure manometer can be used either to adjust automatically the rate of circulation to such a value that it maintains the blood pressure at a fixed level or as a limiting device to slow down or stop the circulation in the event of the pressure rising above a limit. Since the rate of circulation ultimately depends on the venous return available and as any excessive suction from the venous pump merely collapses the veins, it is clear that the suction pressure must play an important part in the controlling system. The signal from the venous suction manometer performs the same function in the control of the venous pump as the arterial pressure signal does for the arterial pump—that is, it tends to reduce the speed of pumping as the suction pressure rises, and will bring the circulation to a stop when a limit is reached. Hence a compromise is established—the two pumps working to maintain the blood volume and the arterial pressure, and to prevent the venous suction becoming too great.

This control gear, with its indicating instruments, warning lights, and switches, is housed in a separate trolley. On the control panel of this trolley are arranged the manual and automatic speed-control selectors with meters indicating the rate and pressure at which each pump is working. Another meter indicates the volume of fluid in the oxygenator. Warning lights are placed above the pressure gauges and the fluid volume meter to draw attention to any variations that exceed chosen limits.

Working of the Pump-oxygenator

On the main trolley the pumps and oxygenator are arranged so that easy access to them is possible. The oxygenator lies on rollers in a recess in the top of the trolley and is covered by a transparent hood. Within this recess a constant temperature can be maintained by warm air, heated by infra-red lamps and circulated by a fan under thermostatic control. Oxygen and carbon dioxide are delivered to the oxygenator through rotameters which allow adjustments of flow rate to maintain the appropriate carbon dioxide tension. The gases pass through a warming, filtering, and humidifying system and then traverse the oxygenator in the opposite direction to that of the blood. A device

for automatically controlling the gas mixture from the *p*H of the blood in the machine is under construction, but is not at present fitted to the machine.

All the tubes enter and leave the oxygenator at one end of the trolley in close proximity to the two pumps (Fig. 9). Connecting blocks at this end of the trolley facilitate the various junctions in the tubing. The arterial block acts both as a coarse filter and as a bubble trap from which bubbles may be returned to the oxygenator through a by-pass tube, which passes through a clamp controlled by a solenoid operated from the control panel. This clamp also acts as a relief valve in the event of a sudden blockage in the arterial line. Connexion to the arterial manometer is also made from the arterial connecting-block.

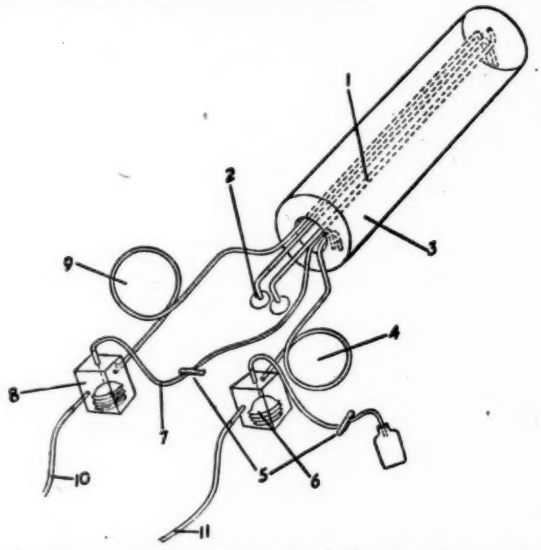

FIG. 9.—The general arrangement of the oxgenator, pumps, manometers, and tubing connexions. 1, Gas entry. 2, Oxygenator level manometer. 3, Oxygenator. 4, Venous pump. 5, Solenoid clamps. 6, Venous manometer. 7, By-pass tube. 8, Arterial filter block and manometer. 9, Arterial pump. 10, "Artery." 11, "Vein."

From the venous connecting-block a tube goes to a reservoir from which the machine is charged and from which transfusions may be made. The tube passes through another electrically operated clamp controlled from the control panel. A second tube connects the venous line to the venous suction manometer.

The tubing in the circuit is of "portex" P.V.C. (polyvinyl-chloride), and is used but once. Before use it is treated with Dow Corning "dimethyl-dichlorosilane" to ensure that the surface is completely non-water-wettable. The arterial catheters are fashioned from this tubing, which is softened by immersion in boiling glycerin and drawn out into a convenient taper, after which rapid cooling fixes the tube in this shape. It can then be hardened by immersion in ethyl ether for 24 hours.

"Polythene" or portex is equally suitable for the venous catheter. Numerous side holes punched in this tube provide efficient collection of blood from the thin-walled veins by gentle suction.

Results of Tests

The machine is efficient, reliable, and comparatively easy to operate. *In vitro* tests confirm that it adequately fulfils the design criteria.

The volume of blood required to charge the machine has been varied between a minimum of 0.5 litre and a maximum of 2 litres without affecting the efficiency of operation.

When stored blood was used it was possible to introduce approximately 100 volumes of oxygen into each litre of blood flowing through it. At 2 litres a minute an average figure is 205 c.cm. of oxygen uptake into stored blood. With fresh blood circulating at 900 ml. a minute, the difference in oxygen saturation between blood entering and leaving the oxygenator was 174 volumes per litre, indicating an uptake of 156 c.cm. of oxygen a minute. At this time the oxygenator was rotating at 60 revolutions a minute.

The average amount of haemolysis in 500 ml. of stored blood circulated for two hours at rates of up to 2 litres a minute was 0.1 g. Hb per 100 ml. When fresh blood was circulated at a rate of approximately 1 litre a minute the haemolysis was rarely detectable to the naked eye and did not exceed 0.05 g. Hb per 100 ml. an hour.

Foaming is not a serious problem, though it will occur if many air bubbles are carried into the oxygenator in the ingoing blood. This foam does not affect the rate of oxygenation, but may increase the rate of haemolysis. It can be prevented by ensuring that the tubes on the suction side are air-tight. If a film of Dow Corning "antifoam A" is deposited over the interior of the machine no foaming occurs whatsoever in spite of injecting foam into the oxygenator.

The servo mechanism controlling the operation of the pump will maintain the blood volume within 50 ml. over a speed range between 300 ml. and 3 litres a minute. It will adjust the pumping rate in response to the pressure manometers, and when one pump is suddenly stopped will bring the other to a standstill within a volume change of 150 ml. The electronic mechanism possesses remarkable stability, and during trials extending over several days, when the apparatus was called upon to repeat frequently, without adjustment, an elaborate series of tests, it proved faultless. The method of construction allows various forms of servo control to be employed by altering the interconnexions between the various units.

Cleaning is effectively carried out after dismantling the apparatus, including all the washers and plates within the oxygenator. It has been found more economic to replace the tubing after each perfusion, though this is not absolutely necessary. As the entire surface with which the blood is in contact is of inert plastic material and the "intima" non-water-wettable, very little deposition of fibrin and other proteins occurs. This property also reduces the amount of anticoagulant required to maintain the fluidity of the blood. At present the oxygenator must be sterilized with chemical agents, for perspex deforms at 100° C. However, this material is being replaced by nylon or teflon, when it will be possible to autoclave in one unit everything in contact with blood.

An extensive series of animal experiments has amply confirmed that the performance under these conditions is in no wise different from that *in vitro*, and justifies the further development of this prototype heart–lung machine.

I am indebted to Professor C. Crafoord and Dr. V. O. Björk for their kindness during my visit to Stockholm in 1949, when I greatly benefited from their experiences in this field. Also I wish to acknowledge the important contributions of the many who have helped in the design and construction of this machine, particularly Mr. R. L. G. Rainbow, Mr. C. Lordon, and Mr. J. Neal, of the Postgraduate Medical School, Mr. Schranz, of the Genito-Urinary Co., Ltd., and Mr. Kellerman and Mr. Brown, of New Electronic Products Ltd. The design of the control gear was carried out by Mr. Brown, who will describe the mechanism in detail elsewhere. Patent applications have been filed and assigned to the National Research Development Corporation.

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EXPERIMENTAL PHYSIOLOGY OF A HEART-LUNG MACHINE IN PARALLEL WITH NORMAL CIRCULATION*

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Recognizing the magnitude of the task involved in the mechanical maintenance of the entire circulation in humans, we turned our attention to the lesser problem of assisting the natural circulation by shunting part of it from vein to artery through the heart–lung machine. To assess the value of the heart–lung machine in resuscitation and in the treatment of a failing circulation, and to acquire information to be applied later to the problem of complete artificial maintenance of the circulation in man, a series of experiments was carried out in dogs.

In the planning and execution of these experiments we were helped by experience gained from a large number of studies carried out with earlier machines. These studies included the perfusion of isolated organs, which proved particularly valuable in providing the basis of the present technique, and enabled controlled conditions to be established.

The Experiments

Thirty greyhound dogs, each weighing between 20 and 30 kg. and apparently healthy, were used. They were dewormed and given intramuscular penicillin (300,000 units 8-hourly) for two days prior to the day of an experiment, when each dog was anaesthetized with intraperitoneal pentobarbitone sodium (30 mg. per kg. body weight). A cuffed tube was introduced into the trachea and inflated, and was then connected to a Benedict–Roth spirometer containing oxygen. Electrocardiograph leads were fixed to the two fore-limbs and to the right hind-limb.

A small incision was made in the neck, and an external jugular vein and a carotid artery were exposed. A radio-opaque catheter was then introduced into each of these vessels and was guided under fluoroscopic control into the right auricle and the ascending aorta or left ventricle respectively. The catheters were connected to continuously recording manometers and arranged so that blood samples could be obtained from them. The patency of each was maintained by flushing with saline which contained heparin (2 mg. per 100 ml.).

One or other deep femoral artery was exposed together with one of the major branches of a femoral vein. A tapered plastic catheter was then introduced into the deep femoral artery and connected to the "arterial" tube of the heart–lung machine. A plastic catheter 25 cm. in length, with numerous side openings, was passed into the femoral vein and advanced until its tip was judged to rest within the thoracic portion of the inferior vena cava. Connexion was made between this catheter and the "venous" tube of the heart–lung machine.

Concurrently with the preparation of the animal the machine was being assembled and made ready for perfusion (see Appendix I). In the first five experiments it was charged with approximately 750 ml. of donor dog's blood, but subsequently, because facilities for sterile blood collection proved inadequate and no definitive method could be achieved for cross-matching mongrel and greyhound blood, a solution of 6% dextran in normal saline was used.

The animals were now given heparin or dextran sulphate (Walton, 1951), 1–2 mg. per kg. being used. Primary readings were then made of the arterial and central venous pressures, the oxygen consumption, and the electrocardiograph, which were then recorded con-

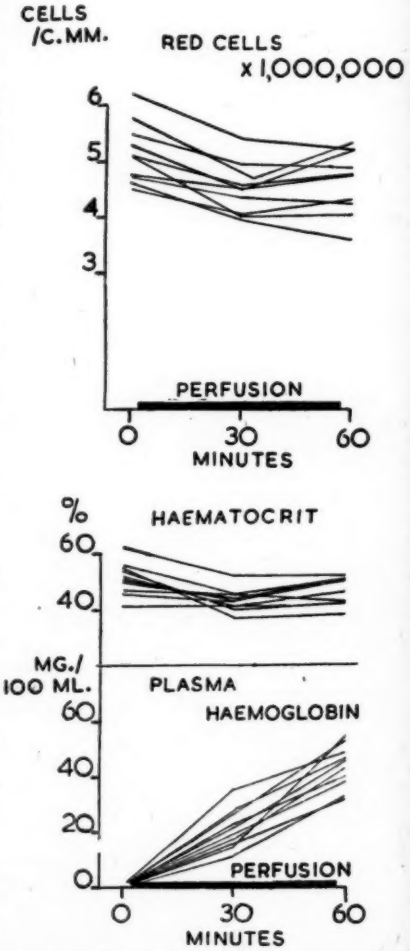

FIG. 1.—Red-cell count, haematocrit, and plasma haemoglobin in 10 dogs before, during, and immediately after one hour's perfusion.

*This work was carried out at the Buckston Browne Research Farm, Kent, by permission of the President and Council of the Royal College of Surgeons of England.

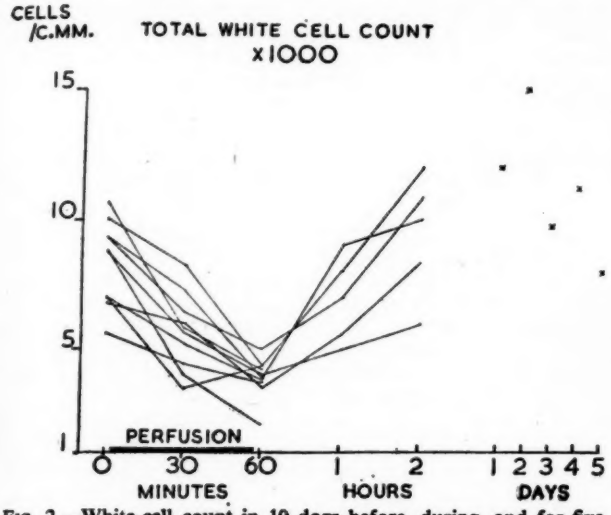

FIG. 2.—White-cell count in 10 dogs before, during, and for five days after one hour's perfusion.

tinuously. Arterial and venous blood samples were also obtained. On these samples were made the following determinations, using standard techniques (Appendix II): (1) arterial and venous blood oxygen content; (2) counts of red cells, platelets, and leucocytes, including the differential and Arneth counts; (3) haematocrit and plasma haemoglobin; (4) plasma sodium, potassium, and chloride, sugar, urea, and carbon-dioxide combining power; and (5) *p*H.

The heart–lung machine was now started and adjusted to circulate at 50–100 ml. a minute, and then increased in rate gradually to between 750 and 1,000 ml. a minute. In most experiments the perfusion was continued for a standard time of one hour, blood samples being taken at intervals during this time and again ten minutes after it had ended. When the final measurements had been made the cannulae were removed, the carotid artery and external jugular vein ligated, and the femoral artery and the vein repaired or ligated. Protamine sulphate was given to neutralize the heparin effect and the dog was allowed to recover consciousness. Subcutaneous vein blood samples were subsequently taken hourly for two hours and then daily for five days, and on these samples a full leucocyte count was carried out.

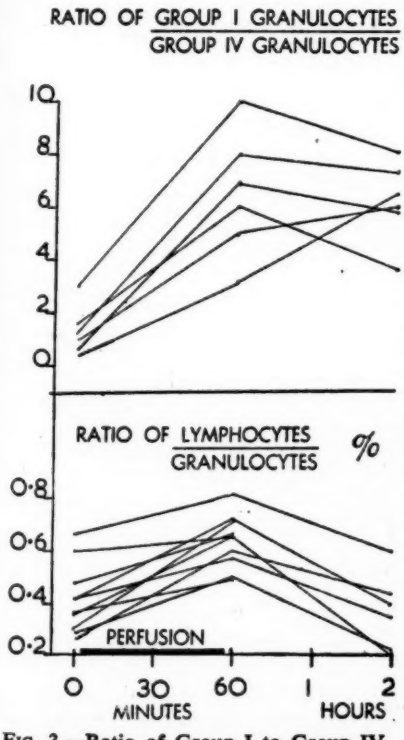

FIG. 3.—Ratio of Group I to Group IV granulocytes in six dogs and the ratio of lymphocytes to granulocytes in 10 dogs before, during, and for two hours after perfusion.

The results of the experiments are considered under four headings: (1) clinical assessment of the effect of the procedure and analysis of morbidity and mortality; (2) the changes in the blood itself while circulating through the machine; (3) the general circulatory effects produced by the artificial circulation; and (4) evidence of the efficiency of the machine as an extrapulmonary oxygenator.

Clinical Assessment of the Procedure

No death directly attributable to the extracorporeal circulation occurred in the 30 dogs studied. Four dogs did not survive the procedure. Two died on the operating table as a result of misjudgments, one from an uncontrollable haemorrhage, and another from a period of asphyxia purposely induced to initiate anoxic collapse of the circulation. One died after prolonged hypotension which began immediately after the perfusion had started and which was probably the effect of donor blood, and one died of peritonitis following intraperitoneal pentobarbitone sodium anaesthesia.

Assessment of recovery from the procedure was complicated by the fact that in 18 cases the femoral artery was ligated and the leg in question temporarily immobilized. A greyhound is reluctant to get to its feet in these circumstances, but clinically measurable dysfunction was absent in all of the 26 animals which survived. After two to three days the dogs were normally active. When arterial repair was successful (six cases) and when the blood had returned into the superior vena cava (two cases) activity became normal within 12 hours. Twenty-five dogs were observed for periods up to three months, and were sacrificed in good condition. Post-mortem examinations did not reveal any abnormalities. One animal preserved as a pet is in such good condition that he has recently sired progeny destined for competitive coursing.

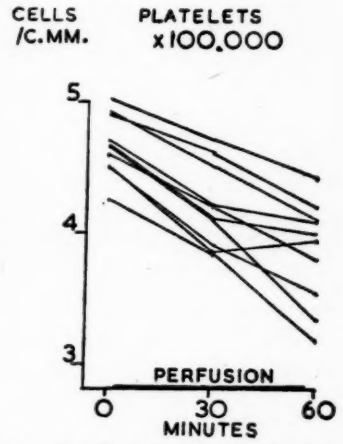

FIG. 4.—Platelet count in 10 dogs before, during, and immediately after perfusion.

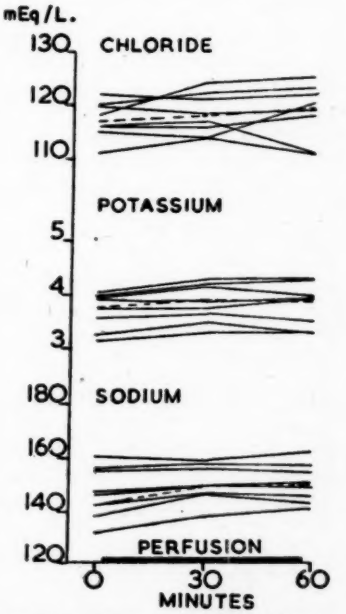

FIG. 5.—Plasma chloride, plasma potassium, and plasma sodium in 10 dogs, before, during, and immediately after perfusion.

Effect of the Machine on the Blood

The most notable effect of the machine on blood circulating through it was on the cellular elements. After one hour's perfusion in 10 dogs the average red-cell count fell from 5,150,000 to 4,500,000 per c.mm., the average haematocrit fell from 51 to 46%, and the average plasma haemoglobin concentration rose to 43 mg. per 100 ml. (Fig. 1).

A dramatic fall occurred in the number of circulating white

cells during the same time (Fig. 2)—from an average primary value of 8,200 per c.mm. to an average value of 4,800. The greatest fall recorded was from 8,800 to 2,100 per c.mm. One hour after cessation of perfusion the average value had risen again to 6,000, and one hour later it had become 8,800 per c.mm. A leucocytosis persisted for five days in all animals.

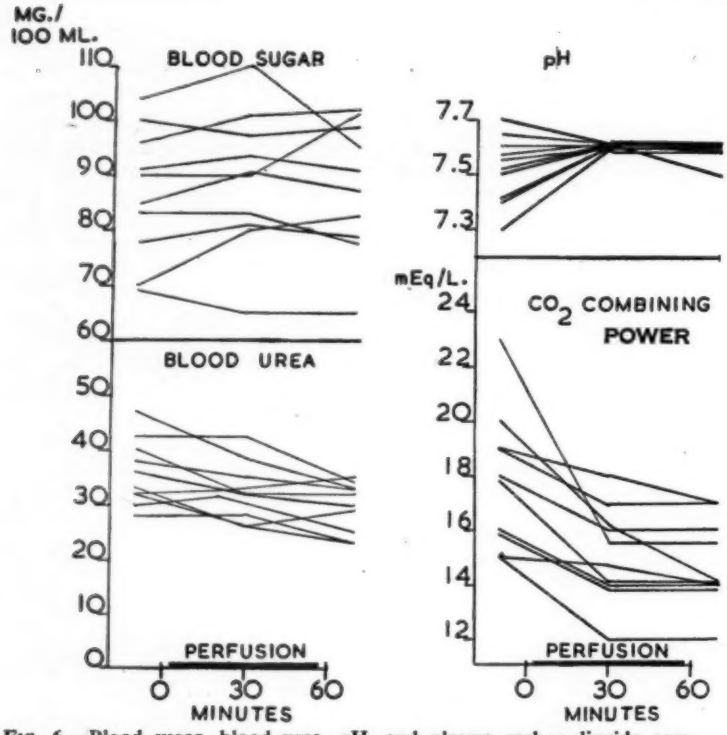

FIG. 6.—Blood sugar, blood urea, *p*H, and plasma carbon-dioxide combining power in 10 dogs before, during, and immediately after perfusion.

The differential count, expressed as the ratio of lymphocytes to granulocytes, and the Arneth count, expressed as the ratio of Group I granulocytes to those of Group IV granulocytes (Fig. 3), showed, after 60 minutes' perfusion, a rise in the average lymphocyte:granulocyte ratio from 0.39 to 0.6, and a marked rise from 1.3 to 7.8 in the average ratio of Group I granulocytes to Group IV granulocytes. This indicated that the fall in white cells particularly affected the granulocytes, and that the more elderly are more greatly affected than the less-developed ones. Two hours after perfusion the ratio of lymphocytes to granulocytes had fallen again to 0.36, but the ratio of Group I to Group IV granulocytes had remained elevated at 6.2.

The platelet count fell from an average value of 463,000 per c.mm. in one hour to an average value of 378,000 (Fig. 4).

In contrast to the cellular elements the plasma electrolytes were relatively unaffected. After one hour's perfusion the average plasma sodium had increased from 149 to 156 mEq per litre, the average plasma chloride from 116 to 120 mEq per litre, and the average plasma potassium from 3.6 to 4.0 mEq per litre (Fig. 5). During the same time the average plasma carbon-dioxide combining power had fallen from 18.0 to 16.0 mEq per litre, while the *p*H had risen from an average of 7.5 to an average of 7.6 (Fig. 6). No significant change was recorded in the measurements of blood sugar and blood urea, the former falling from an average value of 86 to 82 mg. per 100 ml. and the latter falling from an average value of 36 to 30 mg. per 100 ml. (Fig. 6).

Determinations of the plasma proteins were invalidated by the use of dextran.

Effect of the Machine on the Circulation

In the first five experiments, when donor blood was used, the initial delivery from the machine produced a fall in arterial blood pressure which persisted throughout the perfusion. In the remainder, when a solution of dextran in sodium chloride was used, the introduction, maintenance, and termination of the perfusion was accomplished without untoward events, the blood pressure, pulse, and respiratory rates remaining virtually constant.

Electrocardiograph tracings revealed no changes other than an occasional alteration in cardiac rate. No arrhythmias were induced even when the perfusion was started or stopped suddenly.

The cardiac-output changes deduced by application of the Fick principle to the measurements of oxygen consumption and arteriovenous oxygen differences are well exemplified in the detailed consideration of Dog No. 20. This dog remained evenly narcotized throughout two and a half hours. Respiration was deep and regular, and before the beginning of the perfusion the oxygen consumption was 140 c.cm. a minute, the cardiac output 3.2 litres a minute, the mean arterial pressure 115 mm. Hg, and the central venous pressure +2 cm. H_2O. Three minutes after perfusion at 750 ml. a minute the oxygen consumption had fallen to 115 c.cm. a minute and the central venous pressure had fallen to −1 cm. H_2O. The mean arterial pressure had not altered. After 30 minutes the oxygen consumption had fallen to 85 c.cm. a minute and the cardiac output to 2 litres a minute. The mean arterial pressure was then 118 mm. Hg and the central venous pressure +1 cm. H_2O. Just after perfusion stopped the oxygen consumption rose to 160 c.cm. a minute for four minutes and then fell to 95 c.cm. a minute during the succeeding five minutes. At this time the cardiac output was 2.3 litres a minute, the mean arterial pressure 115 mm. Hg, and the central venous pressure +2 cm. H_2O.

Similar determinations of cardiac output were carried out in 12 dogs (Fig. 7). In nine the cardiac output fell during perfusion, in one it remained unaltered, and in two it rose. In seven of the nine dogs in which the cardiac output fell the extent of the fall approximated the rate of perfusion, averaging 850 ml. a minute.

Evidence of Efficiency of the Machine as an Extrapulmonary Oxygenator

Oxygen can undoubtedly be introduced into a recipient's blood stream by means of the heart–lung machine. In a single dog, for example, there was an oxygen difference of 15 vols.% between the venous blood entering the machine and the arterialized blood leaving it. And, since the rate of blood-flow through the machine was 1 litre a minute, approximately 150 c.cm. of oxygen a minute was introduced.

In order to determine if benefit followed from the extrapulmonary addition of oxygen six dogs were made anoxic by reducing the concentration of oxygen in the inspired air, replacing it with nitrogen. Venous blood, removed from the distal inferior vena cava, was returned after arterialization into the femoral artery in two dogs, into the thoracic aorta in two dogs, and into the superior vena cava in two dogs. The rate of perfusion did not exceed 1 litre a minute.

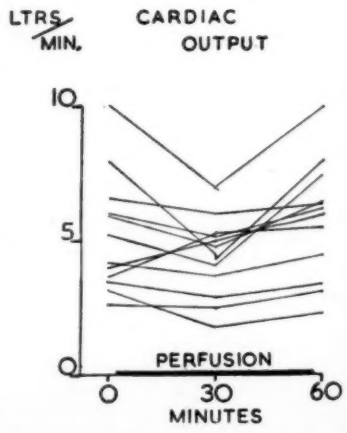

FIG. 7.—Cardiac output in 12 dogs before, during, and immediately after perfusion.

In each case oxygen was introduced into the circulation, but striking differences were revealed in the three pairs of dogs (Fig. 8). In the first two dogs, when the perfusion was returned into the femoral artery, there was little apparent effect on the oxygen content of the carotid artery blood, and the cephalic end of the dogs remained anoxic. After the animals had been breathing pure nitrogen for ten minutes the oxygen content of this blood had fallen to 23%. At the same time, however, the caudal end received an abundance of oxygen from the artificial lung, blood returning to the machine from the distal inferior vena cava being 65% saturated.

The perfusion was stopped at this point and complete anoxia maintained until cardiac arrhythmia and respiratory arrest had occurred. Resumption of the perfusion then restored respiration in both dogs and induced a normal heart-beart in one. The oxygen content of the carotid-artery blood was at this time identical with that of blood leaving the machine. In the second animal the heart ceased to beat after a short period of ventricular fibrillation, but perfusion was continued for two and a half hours, during which time natural respiration continued and the tongue and pupillary reflexes remained active.

In the second two dogs, in which the artificial circulation was returned into the aorta proximal to the splanchnic and renal arteries, a good perfusion of the cranial vessels was obtained, and the carotid-artery blood content did not fall below 50% even when pure nitrogen had been inspired for ten minutes.

In the last two dogs, in which arterialized blood was returned into the superior vena cava, the carotid-artery blood content was 52% ten minutes after exclusion of oxygen from the inspired air.

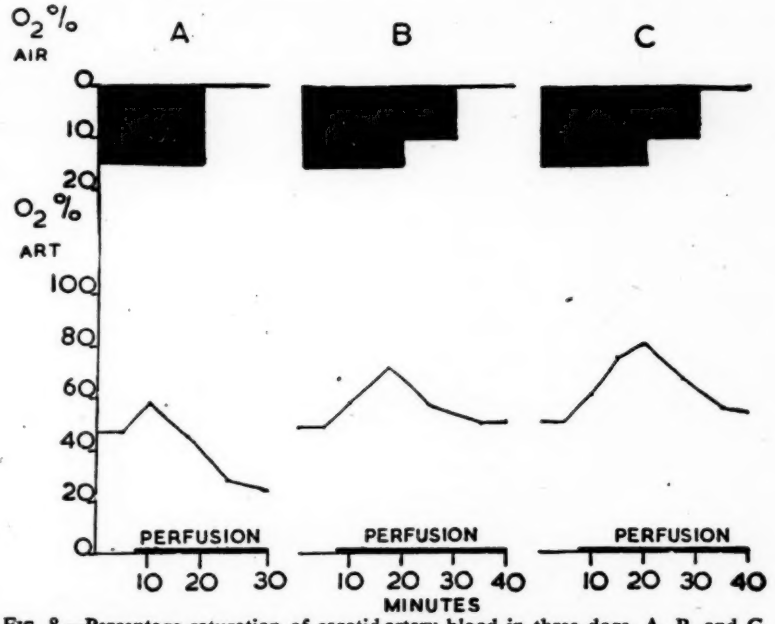

FIG. 8.—Percentage saturation of carotid artery blood in three dogs, A, B, and C, in which anoxia was induced by reduction of oxygen in the inspired air. Artificially arterialized blood was returned into the femoral artery in A, into the thoracic aorta in B, and into the superior vena cava in C.

Discussion

The use of 6% dextran in sodium chloride to charge the heart–lung machine greatly contributes to its effective application to animal experimentation. The collection of blood from donor dogs, and its accurate cross-matching, is a difficult problem. In the five experiments in which donor blood was used, hypotension occurred when the contents of the machine were introduced into the circulation. We were not able to account for this, and it was concluded that an unknown factor in the donor's blood was responsible. The barbiturate used to anaesthetize the donor, the presence of products associated with exsanguination, bacterial contamination, and serological and cellular incompatibility were all possibly implicated.

No effects other than haemodilution and a resulting anaemia followed the use of dextran solution. The fall in the number of red cells is undoubtedly due to this deliberate haemodilution, for were the sole cause haemolysis the fall would not have exceeded 0.3%, and would not have been measurable. Of course it may be argued that no account is taken in the calculation of the fact that haemolysed blood may be fixed in the tissues. However, even if a figure of 200 mg. per 100 ml. is taken as the level of haemolysis, a figure considerably larger than any found in *in vitro* experiments, the fall in the red-cell count would only be in the order of 1%.

The amount of haemolysis is of no real consequence. No deleterious effects are to be expected from the liberation during perfusion of relatively minor quantities of haemoglobin. Much greater amounts have been administered to human beings without harm (O'Shaughnessy, Mansell, and Slome, 1939).

Deliberate haemodilution also accounts for much of the fall in the number of circulating platelets, which is too small to be of significance, but it cannot be responsible for the magnitude of the change in leucocyte values. Considerable destruction of circulating white cells does occur, and the resulting leucopenia may constitute a grave impediment to continuous perfusions over long periods. This problem is being studied at the present time, though it is evident that perfusions of short duration, such as are reported, need not be rejected on account of their effect on the leucocytes.

The alterations in the electrolyte balance are of a very small order, and in the main are caused by the addition of unbalanced fluids to the circulation, and by the absence of an accurate means of adjustment of the carbon dioxide tension in the oxygenator. The first is easily rectified, the second awaits the development of a device capable of regulating the carbon dioxide tension from the *p*H of the circulating blood. A device of this nature has been successfully exploited by Miller, Gibbon, and Gibbon (1951).

No untoward physiological effects accompany the shunting of a part of the natural circulation through the heart–lung machine. Changes in arterial pressure, pulse, and respiration rate are slight, and animals appear clinically unaffected by the procedure. Cardiac output determinations seem to indicate that a fall occurs when the perfusion is running, though it would not be wise to claim too much from these results, which are not statistically significant. In carrying out these determinations much difficulty was encountered in establishing a satisfactory baseline, particularly when pentobarbitone sodium was used as an anaesthetic. The smallest variation in the depth of narcosis altered the cardiac output, and we rarely achieved a uniform depth throughout the procedure. Even though the doses of pentobarbitone sodium were adjusted according to the weights of the animals the dogs did not all react in the same fashion. In some the dose was more than enough and produced deep anaesthesia, while in others it did no more than produce light narcosis. Even when anaesthesia was produced by cyclopropane, administered by a skilled anaesthetist, three hours of carefully regulated anaesthesia was required before two consecutive cardiac outputs proved to be identical.

Oxygen can be introduced into the blood stream by this method, and the extrapulmonary addition is of benefit to dogs made anoxic by a reduction of oxygen in the inspired air. The site of return of artificially arterialized blood is of great importance, and should be either into a central vein or into an artery close to the heart.

For these reasons it is felt that the heart–lung machine is now ready for clinical trials in selected cases of extreme cardio-respiratory dysfunction. In those patients in whom derangement of pulmonary function is the chief symptom, it may be advantageous to return the arterialized blood into a central vein, thus greatly simplifying the cannulation and making the surgical intervention a relatively minor one. Though no shunting of blood around the heart would occur in this technique, it is possible that the improved oxygenation would reduce the demands on the heart, and secondarily reduce its work.

Where the myocardium is primarily involved it is suggested that continuous venesection with return of arterialized blood into the arterial circulation will relieve the heart of part of its burden.

APPENDIX I

The oxygenator and connecting-blocks were chemically sterilized with "roccal" detergent and 3% formalin, being steeped in the solution for twelve hours. The tubing and cannulae, which we used only once, were autoclaved. After assembly the apparatus was washed with at least 40 litres of sterile distilled water to which had been added enough sodium chloride to provide approximate isotonicity. Frequent checks for the presence of formalin provided an indication of the efficiency of the washing process. When two checks were negative the wash-outs were discontinued and the apparatus was charged with donor blood or dextran solution. After circulation through the by-pass tube to ensure that no air bubbles remained in the arterial line, the machine was ready for use.

APPENDIX II

1. The arterial and venous blood oxygen were measured by the method of Van Slyke and Neill (1924).

2. The red-cell, platelet, leucocyte, differential, and Arneth counts were made, and haematocrit values found by standard methods (Dacie, 1950).

3. The plasma haemoglobin was estimated as oxyhaemoglobin on a Spekker absorptiometer modified to accept 1 by 6 in. (2.5 by 15 cm.) test-tube cuvettes. A standard oxyhaemoglobin curve was prepared for each estimation in the following manner: 3-ml. aliquots of plasma were placed in each of five cuvettes; to the first was added 8 ml. of dilute ammonia reagent (5 ml. concentrated NH_3 per litre), and this served as a plasma blank; to the remainder was added 0.02, 0.04, 0.06, and 0.08 ml. of whole blood diluted 1 in 2 with normal saline; these were then diluted with 8 ml. of ammonia reagent and read against the plasma blank. 3 ml. of plasma obtained from samples taken during the experiment was similarly treated and compared with the standard curve.

4. The plasma sodium and plasma potassium were determined by means of an internal standard flame photometer similar to that described by Berry, Chappell, and Barnes (1946).

5. The plasma chloride, plasma CO_2 combining power, blood sugar, and blood urea were estimated by standard methods (King, 1951).

6. The *p*H was measured by a Muirhead *p*H meter type D-303-b.

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POST-INOCULATION POLIOMYELITIS

BY

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The successful prophylaxis of diphtheria through the mass immunization of very young children with diphtheria toxoid was associated with few mishaps of importance. When given subcutaneously, the alum-precipitated toxoid commonly gave rise to a painless nodule which was gradually absorbed, but occasionally there was an inflammatory swelling and very rarely a sterile abscess. These rare reactions to the toxoid were minimized by intramuscular administration, a route which was necessary for the injection of the pertussis vaccine introduced in 1946 and of combined diphtheria toxoid and pertussis vaccine made available in 1947. Since then the latter product has been increasingly used to immunize children simultaneously against diphtheria and whooping-cough by one series of injections.

In 1948 Martin (1950) observed flaccid paralysis of the arm in two children, each of whom had received an inoculation of a prophylactic in the paralysed limb within the preceding three weeks. Having traced and studied 15 other patients who had developed limb paralysis following injections of antigens in 1944–9, he concluded that all of these had really suffered from poliomyelitis. Gale (1950) was able to add 56 cases of limb paralysis following the inoculation of prophylactics, and then, independently and simultaneously, McCloskey (1950) and Geffen (1950) published their findings during two epidemics of poliomyelitis in 1949. In Melbourne, McCloskey found that 35 out of 340 patients with poliomyelitis had been inoculated against diphtheria or whooping-cough within three months before the onset of the illness, and that the paralysis affected the inoculated limb in 24 out of 31 patients about whom full information was obtained. Geffen reported that out of 182 poliomyelitis patients under 5 years of age in London, 37 had been recently inoculated and about 30 of these suffered from paralysis, affecting particularly the limb recently injected. Investigating a small group of the London children, MacCallum (1950) was able to isolate the poliomyelitis virus from the stools of two children with paralysis of a recently inoculated limb and from three other inoculated children suffering from poliomyelitis without paralysis. Hill and Knowelden (1950) carried out a statistical inquiry, covering 33 areas, into the incidence of paralysis as a sequel to recent inoculation in 1949, and concluded that this misfortune occurred more frequently within a period of one month after the inoculation than could be attributed to chance.

On the other hand, Culley (1951) could find only nine recently inoculated persons among the 380 Welsh

patients with poliomyelitis in 1950 and only four of the nine with paralysis in the inoculated limb. In Scotland, Sutherland (1952), studying 43 cases of poliomyelitis following inoculation in 1950, could not show that inoculation increased the risk of a child developing poliomyelitis, although he found that the paralysis was suggestively but not significantly associated with the limb most recently injected. From both the academic and the practical point of view, the present position is best summarized in the advice of the Chief Medical Officer of the Ministry of Health (1952), that in any area in which poliomyelitis is exceptionally prevalent inoculation of diphtheria and pertussis antigens should be suspended for a time.

Poliomyelitis on South Tyneside

In the spring of 1952 a local epidemic of poliomyelitis began on Tyneside, centred mainly on the south side of the river. This outbreak witnessed the resumption of the classical age distribution of the disease, for two-thirds of the patients were under the age of 5 years. The districts chiefly involved were Gateshead (population 115,000), and the contiguous districts of Felling (population 25,286) and Whickham (population 23,116). Poliomyelitis was confirmed in 91 patients from Gateshead, 28 from Felling, and 13 from Whickham. All these districts are normally served by Sheriff Hill Isolation Hospital, in which 112 of the patients were treated along with six cases from other areas.

In the last week of March and during April, four children were admitted to hospital at intervals for investigation of an illness which was at first diagnosed as "viral encephalitis" but later revised to polio-encephalitis in the light of further developments. The first patient with unmistakable poliomyelitis became ill with a sore throat on May 2, 1952, and was admitted to hospital on May 6 with flaccid paralysis of both legs. During May, 8 non-paralytic and 2 paralytic cases of poliomyelitis were later admitted from the three districts, to make a total of 15, of whom three were paralysed. Two of the three paralytic children had recently been inoculated. Intramuscular inoculations were therefore stopped in the Gateshead clinics, and local practitioners were advised on June 3 to restrict immunization to the subcutaneous use of A.P.T. and P.T.A.P. Confirmed cases of poliomyelitis in June numbered 38, and it was evident that the infection was widespread throughout the area. In July,

Poliomyelitis Following Inoculations—South Tyneside, 1948–52

Year	Patient and Area	Age in Years	Inoculation			Poliomyelitis		
			Antigen	Date of Injection	Site	Onset	Clinical Summary	Last Assessment
1952	H.S. (G)	11/12	D & P 0·5 ml.	24/4/52 (second)	Left arm	10/5/52	Fever, complete loss of power left shoulder-girdle and arm. Slight movement of fingers. C.S.F., 2 polymorphs per c.mm.	22/9/52: paralysis of left shoulder, extensors of elbow, and flexors of wrists and fingers
	R.H. (G)	1 2/12	D & P 0·5 ml.	16/5/52 (first)	Left buttock	1/6/52	Off feet; drowsy; paresis left quadriceps. C.S.F., pleocytosis and increased protein	2/7/52: complete recovery
	M.J. (G)	1 10/12	D & P 0·5 ml.	20/5/52 (second)	Left arm	4/6/52	Restless; vomiting and retention of urine followed by neck stiffness with paralysis left shoulder and arm, except fingers. C.S.F., increased cells and protein	19/9/52: paralysis and wasting left shoulder muscles, biceps, and triceps
	E.S. (G)	1 4/12	D & P 0·5 ml.	20/5/52 (third)	Right arm	17/7/52	Pyrexia, irritability, neck stiffness with paralysis right shoulder and upper arm. C.S.F., pleocytosis and increased protein	22/9/52: paralysis of right shoulder, biceps, and triceps
	M.B. (G)	4	D 0·5 ml.	17/6/52 (booster)	Right buttock	20/6/52	Headache, fever, neck stiffness, off feet, loss of tendon reflexes right leg but no paralysis. C.S.F., increased cell count only	5/7/52: perfect recovery
	P.H. (W)	5	D 0·5 ml.	5/5/52 (booster)	Left arm	23/5/52	Headache, fever, neck stiffness, pain in left calf, proceeding in 5 days to paresis both arms and left leg. C.S.F., increased cells	9/10/52: normal range of joint movement, but left deltoid muscle very weak
	V.C. (F)	2	D 0·5 ml.	26/6/52 (first)	,, ,,	1/7/52	Vomiting, irritable, listless, paralysis of left external and right internal rectus muscles, with spasm of right neck muscles. C.S.F., increased cells	1/8/52: complete recovery
	A.B. (F)	9	D 0·5 ml.	29/5/52 (booster)	,, ,,	14/7/52	Headache, weakness of legs, and vomiting, frequency of micturition. 17/7/52: paralysis extensors right ankle. C.S.F., pleocytosis and increased protein	12/9/52: slight right foot drop; otherwise walking well
1950	J.L. (G)	1 5/12	D & P 0·5 ml.	31/5/50 (second)	,, ,,	10/6/50	Diarrhoea with paralysis left arm on 16/6/50. Out-patient treatment only	13/9/52: wasting and paresis of left deltoid, biceps, and triceps
	A.P. (Wn)	11/12	D 0·5 ml.	6/7/50 (first)	,, ,,	19/7/50	Earache followed by diarrhoea. 29/7/50: paralysis of both arms with neck stiffness. C.S.F., increased cells and protein	18/9/52: paresis both deltoids, with wasting more marked on left side; slight wasting left thigh and eversion of left foot and slight drag in gait
	A.D. (G)	10/12	D & P 0·5 ml.	31/7/50 (first)	Left thigh	31/7/50	Feverish on 31/7/50, drowsiness, vomiting. 5/8/50: neck stiffness, paresis of left facial muscles, and internal squint of right eye. C.S.F., pleocytosis and increased protein	5/9/50: complete recovery maintained until 1952
	J.T. (G)	11/12	D & P 0·5 ml.	26/6/50 (first)	Left arm	14/8/50	Feverish and vomiting. 16/8/50: paralysis left arm and shoulder. C.S.F., 1·2 polymorphs and 6 lymphocytes per c.mm.	15/9/52: no loss of movement shoulder or elbow, but paresis and wasting left deltoid, biceps, and triceps
1948	K.M. (G)	2	P 1 ml.	25/10/48 (third)	,, ,,	7/11/48	Paralysis left arm and shoulder with irritability and stupor: spread to right arm except fingers on 15/11/48. C.S.F., 2 polymorphs and 3 lymphocytes per c.mm.	17/11/52: no movement of either shoulder-joint—left arm completely paralysed, including all fingers; right arm limited movement of elbow-, wrist-, and finger-joints; severe wasting of paralysed muscles. In special school

Areas: G = Gateshead; F = Felling U.D.; W = Whickham U.D.; Wn = Washington U.D. Antigens: D = Diphtheria; P = Pertussis.

August, and September confirmed cases numbered 50, 19, and 14 respectively, and thereafter only sporadic cases occurred.

In spite of the precautions, eight of the South Tyneside patients with poliomyelitis had previously been injected intramuscularly with an immunizing antigen not more than two months before the onset of the illness. All these were admitted before July 17, when the number of cases was 94.

The relevant details of the inoculated children are summarized in the Table on the previous page along with similar data relating to five examples of post-inoculation poliomyelitis in 1950 and 1948. Four were recorded among the 27 confirmed poliomyelitis cases on South Tyneside in 1950, while the fifth was a solitary patient who came to hospital two months after the notification of the last case in 1948.

After the end of May, 1952, 101 children were inoculated subcutaneously with A.P.T. and P.T.A.P., but none of these suffered an attack of poliomyelitis.

Comparative Incidence of Poliomyelitis in Recently Inoculated and Other Children in Gateshead in 1952

The total number of children aged 6 months to 2 years in the borough in mid-year, 1952, has been calculated from the births less deaths to be 3,097, among whom there were 17 cases of poliomyelitis, a ratio of 1 in 182. Of the 17 children, 13 presented some degree of muscular paralysis.

In April and May, 1952, 249 children, aged between 6 months and 2 years, received intramuscular arm injections in the Gateshead local authority clinics, and 105 others within the same ages received intramuscular inoculations from local practitioners in April, May, and early June—that is, a total of 354. Of this number, three aged from 11 to 22 months developed poliomyelitis in the paralytic form before the end of June.

Deducting the 354 inoculated children from the total, children of the same age not recently inoculated number 2,743, of whom 9 developed poliomyelitis in May and June, 6 being affected by muscular paralysis. The attack rate in recently inoculated children was therefore 1 in 118, as compared with 1 in 305 in non-inoculated children. During July another case of paralytic poliomyelitis occurred in a recently inoculated child and 3 cases in the control group, of whom two were paralysed. The comparative incidence in May, June, and July was therefore 1 in 88 for the recently inoculated and 1 in 228 for the control group. As an additional paralytic case occurred in the control group in August, the respective attack rate over the four months May to August remained 1 in 87 among the recently inoculated and increased to 1 in 211 in the controls.

Two of the children, E.S. and N.S., who developed a limb paralysis following an injection of antigen in April were previously inoculated in March, both in the left arm. Although these March injections were given one week before the first case of poliomyelitis in 1952, and E.S. was paralysed in the right arm, it seems advisable to recalculate the incidence of the disease in children inoculated in the months March to June.

In March, 53 children of the age group under study received intramuscular inoculations at the clinics and 43 others received similar injections from the general practitioners. Out of 450 children inoculated in the months of March, April, May, and June, 3 developed poliomyelitis in May and June, giving a ratio of 1 in 150. Of 2,647 children of the same age who had not been recently inoculated 9 developed poliomyelitis in these months, a ratio of 1 in 294. When this comparison is extended to include July there were 4 cases in the inoculated, or 1 in 112, and 12 cases among the others, or 1 in 221. Including the August case among the controls, the respective incidence rates for May to August were 1 in 112 for the inoculated and 1 in 204 for the others. As no other child of these ages contracted poliomyelitis, the last-mentioned attack rates cover the whole epidemic. The 13 children in the control group who contracted poliomyelitis were aged from 6 months to 1 year and 10 months. Only two of them had in fact ever been inoculated, the prophylactic injections having been given in the autumn of 1951. In spite of the smallness of these numbers, I feel that they are reasonable in assessing the risk of a child developing poliomyelitis as being at least doubled as a result of intramuscular immunization during an epidemic.

In the 4 recently inoculated Gateshead children the paralysis was limited to the injected arm in three instances and the injected leg in one. In contrast, the 9 patients with paralytic poliomyelitis among the control group of Gateshead children suffered paralysis affecting the trunk and all the limbs in two cases (one of whom died), the right arm, leg, and facial muscles in the third, the left face, eye, and leg in a fourth, one leg only in four instances, and the left external rectus muscle of the eyeball in the ninth.

Poliomyelitis in Recently Inoculated Persons

Analysis of the form of the disease in the 138 South Tyneside cases, so as to compare the recently inoculated patients with the remainder, gives this result:

Form of disease	Recently Inoculated	Others
Non-paralytic	1	70
Paralytic:		
Cranial nerves only	1	15
One arm only	3	3
One leg only	2	17
Both legs	—	7
Arms and legs	1	3
Trunk and limbs	—	6 (2 died)
Cranial nerves and limbs	—	5
Cranial nerves, trunk, and limbs	—	4 (1 died)
	8	130

Among the recently inoculated patients, paralysis affected solely the inoculated arm in 3 patients, the inoculated leg in one, and extended from the inoculated arm of a fifth patient so as to involve the opposite arm and a leg. In two patients paralysis was localized to the ocular muscles and to the right leg respectively, although the injection had been given in the left arm. Only 60 of the 130 patients not recently inoculated suffered a paralysis, and this much more often affected the legs than the arms.

Health of Contacts

As it is well known that poliomyelitis becomes manifest in only a small proportion of the individuals who have been infected, it is common to find that familial contacts of patients suffer from illnesses which are presumably abortive attacks of poliomyelitis. It is rare, however, in urban areas to find two cases of undoubted poliomyelitis from the same family.

Among the 8 families of children with post-inoculation poliomyelitis two, those of E.S. and P.H., are notable for associated illnesses.

Family of E.S.—E.S., aged 1 year, was inoculated in the left arm on February 12 and March 11, 1952, and in the right arm on May 20, with combined antigen. She became ill on July 17 with paralysis of the right shoulder and upper arm. She was admitted to hospital on July 18 along with a brother Eric S., aged 6 years, who complained of headache and vomiting on July 17. On admission he presented an inflammatory exudate on the tonsils, a temperature of 100.6° F. (38.1° C.), but the cerebrospinal fluid was normal. He was considered to be a possible atypical case of poliomyelitis. Two weeks before, an older brother, H.S., aged 11 years, was ill with a high temperature lasting for 24 hours.

Family of P.H.—P.H., aged 5 years, inoculated in the left deltoid on May 5, 1952, with a "booster" dose of A.P.T., became ill on May 23 and was admitted to hospital on the 25th with pyrexia, marked signs of meningeal irritation, and an abnormal cerebrospinal fluid. She developed paresis of both arms and the left leg on May 28, the left arm being the more severely affected. Her sister, M.H., aged 2 years, became ill on May 22, with pyrexia, neck stiffness, and irritability, which persisted until the 28th, when she also was admitted to hospital, making a very rapid recovery in the following three days. In her case the cerebrospinal fluid showed a raised protein content only. Still another child in this house, aged 6 years, complained of pyrexia, headache, and neck stiffness, beginning on May 22, but she was convalescent when her sisters were removed to hospital.

On examining the family histories of the remaining 129 poliomyelitis patients who had not been inoculated recently

there was only one example of two siblings with frank poliomyelitis and one family with a possible double infection.

Family of Sw.—T. Sw., aged 2 years, became ill on July 9, 1952, with drowsiness and irritability accompanied by vomiting. On admission to hospital on July 16 he presented neck and spinal rigidity and loss of the tendon reflexes of the left leg, but he was able to move all his limbs. The cerebrospinal fluid showed an increased cell count and a raised protein content. On July 20 the patient showed a definite weakness of the muscles of the left ankle joint. A sister, G. Sw., aged 4 years, became ill on July 11, with vomiting, fever, and fretfulness, and complained of headache and backache. When admitted to hospital on July 19 there were signs of meningeal irritation but no paralysis. The cerebrospinal fluid showed a pleocytosis of polymorphs and lymphocytes and a raised protein content. This child was fully convalescent on July 27.

Family of M.—The patient D.M., aged 1 year, became fretful and off-colour on August 2, 1952, and was admitted to hospital on August 6, when he presented neck stiffness, minimal pyrexia, and weakness of the right hip muscles, together with a slight increase of cells in the cerebrospinal fluid. This child was not definitely paralysed, but the muscles governing the movement of the joint were all weak. Two weeks previously a sister, aged 3 years, was very restless and had a bout of vomiting, and was thought to have been an abortive case.

Among the 8 households of the recently inoculated patients one can find two with multiple illnesses in the family. In these, the two recently inoculated children suffered paralysis of the injected arm. To find two other instances of multiple illness one has to review the background of the other 129 patients. In these the paralysis affected the lower limb in two children and was slight. It seems probable that all three of the children in each of the households of E.S. and P.H. had been infected with the poliomyelitis virus, and that it was the recent inoculation which determined the appearance and the site of the paralysis.

Intervals between Inoculation and Onset of Poliomyelitis

In 5 of the 8 recently inoculated patients of 1952, paralysis was definitely related to the site of the preceding injection, whereas there was no paralysis in one, and paralysis remote from the inoculation in two. The intervals between the injection and the onset of symptoms in the former patients were 15, 16, 16, 18, and 58 days respectively. In contrast, the respective intervals were 3, 5, and 46 days in the latter three cases. Turning to the 5 patients of 1948 and 1950, the relevant intervals were 10, 13, 13, and 18 days in the cases with paralysis involving an inoculated limb, and in the exceptional case the onset of polio-encephalitis coincided with the inoculation. This divergent finding raises a strong probability that the relationship between the preceding inoculation and the subsequent localized paralysis was one of cause and effect in the group of 8 patients showing intervals of 10 to 18 days between the inoculation and the onset of symptoms, whereas the association was purely a coincidence in the 3 patients in whom the respective intervals between the inoculation and the onset of illness were 5 days or less.

There remain two patients with lengthy intervals between inoculation and illness. In one of these the relationship between inoculation and paralysis may also have been causal.

Site of Injection

In the 1952 group of 8 recently inoculated patients, the upper-arm paralysis following injection tended to be fairly severe and lasting, whereas the paresis of the leg following previous injection of antigen in the buttock was very transient. Studying all the 13 cases of poliomyelitis following recent inoculation, it is notable that antigen given intramuscularly in the arm on 10 occasions was followed by severe paralysis limited to the arm in 5 patients and by more extensive paralysis involving both arms in 3 others. All these 8 patients have or are likely to have some degree of permanent disability. On the other hand, in 3 patients inoculated in the buttock or thigh only one showed paralysis of the injected limb, which was transient. All the 5 post-inoculation cases of paralysis limited to the injected arm were of a severity and permanence not observed in the three single-arm palsies among the 129 patients not recently inoculated, in whom the affected muscles showed a transient loss of power without any residual disability. In the 3 cases of more extensive paralysis following the injection of an arm, paralysis started and was most severe in the injected limb, whence it spread to the opposite arm and thence to other muscles. Although the issue here is clouded by the time relation between inoculation and subsequent illness, the relative severity and persistence of the damage to muscles of the arms in post-inoculation poliomyelitis were impressive.

Prophylactics Used

In the 13 cases of post-inoculation poliomyelitis, paralysis followed the use of diphtheria alum-precipitated toxoid, pertussis alum-precipitated vaccine, and combined diphtheria toxoid and pertussis vaccine.

The dose injected was taken from multiple-dose containers of 5 ml. and 10 ml. Two patients, E.S. and M.J., probably received antigen from the same container, but otherwise each patient was the sole poliomyelitis case associated with a multiple-dose container. The worst case was K.M., to whom the largest dose of antigen, 1 ml., had been given, with a severe local reaction.

During the summer of 1952 many intramuscular injections of penicillin, streptomycin, and other medicaments must have been given to Gateshead patients, both children and adults, in hospital wards and departments and at home, for the treatment of various conditions. In only one instance was there a suspicion that intramuscular injection of a substance other than a prophylactic antigen might have precipitated paralytic poliomyelitis. In this instance, a child of 6 months admitted to hospital with pneumonia on May 30, 1952, was given penicillin by injection into the buttocks alternately before June 5. In convalescence a flaccid paralysis of the right leg was first noticed on June 14, and the cerebrospinal fluid taken on July 21 showed an increase of cells and a slightly raised protein.

Discussion

The Gateshead experience must be added to the London and Melbourne evidence against intramuscular inoculation with diphtheria and whooping-cough antigen as a causal factor in the development of paralytic poliomyelitis affecting particularly the limb previously injected. In Gateshead as in London, the upper limbs were much more frequently affected in the recently inoculated than the legs, and the left arm more often than the right—features quite contrary to the usual distribution of paralysis of poliomyelitis. This can be accounted for only by the traditional use of the left arm for all the immunization procedures.

That the patients with whom we are concerned in Gateshead were in fact cases of poliomyelitis cannot be doubted. They were all diagnosed as such on clinical grounds, for they showed an involvement of the motor neurones and a complete absence of sensory disturbance, together with the changes of the cerebrospinal fluid and many of the common symptoms and signs of this disease. They occurred at a time when poliomyelitis was prevalent, and their numbers were proportionate to the intensity of prevalence. I have, too, been able to cite the simultaneous occurrence of non-paralytic and post-inoculation paralytic poliomyelitis in the same household.

Although mass immunization against diphtheria started in Gateshead in 1941, there were no recorded cases of post-inoculation paralysis among the thousands of children inoculated. This seems to be largely true of the millions of children in the country who were immunized before and after 1941.

The indications are that these mishaps became so numerous as to attract general attention in 1949, a year when poliomyelitis was prevalent in England. Yet in 1947, also a year of high prevalence of this disease, cases of post-inoculation paralysis were very few, if in fact they occurred. It seems that the change in frequency of the misfortune of

post-inoculation paralysis may have been associated with the increasingly popular use of the pertussis vaccine, alone or combined with diphtheria toxoid. It is worthy of note that these antigens were given by the intramuscular route.

Although there is ample room for speculation and research regarding the pathology of post-inoculation paralytic poliomyelitis, the convenient explanation is that muscle trauma due to inoculation enables the virus already present in a patient to attack the motor cells in the spinal cord which innervate the muscles that have been damaged. This would mean that, as a sequel to previous inoculation during the outbreak of poliomyelitis, a number of non-paralytic, atypical, or symptomless cases of infection with the virus would be transformed into frank cases of paralytic poliomyelitis. There would then be an actual increase of the number of cases of paralytic poliomyelitis as a result of the common inoculation procedures. Statistical proof of this increased incidence has not been forthcoming in two national surveys, but this is understandable when one recalls that poliomyelitis seldom shows a national prevalence, and information has to be gathered second- or third-hand about a disease notorious for errors of diagnosis. In a local epidemic it is difficult to get adequate numbers to offset the vagaries of chance.

Difficulties will also arise as a result of the recommended advice to suspend intramuscular inoculation during an epidemic, and there is, too, the further consideration that children who have been recently inoculated may acquire poliomyelitis during an epidemic without this being related at all to previous immunizing procedures. If one could disregard the element of chance in the Gateshead experience of poliomyelitis in 1952, the risk of contracting the disease was doubled, if not trebled, for a child in the age group usually selected for primary immunization. If so, one-third to one-half of all the recorded cases of poliomyelitis following recent inoculation would present the disease as it might have occurred naturally, and the remainder would present the special feature of the localized paralysis in the limb injected. This, in fact, is what did happen to something like the proportions expected, a point which seems to justify the statistical comparison.

In Gateshead, patients developing poliomyelitis less than six days after inoculation were clinically similar to those with the naturally occurring disease, but in those who were inoculated more than 10 days and less than 18 days before the onset of symptoms the inoculated limbs showed the paralysis of the disease. This is in accord with the findings of McCloskey. In two patients with respective intervals of six and eight weeks, the findings were equivocal, but it seems that the effect of the muscle trauma may extend much longer than a period of three weeks.

The practical aspects of this problem require some attention. The advice of the Ministry of Health to suspend intramuscular immunization was acted upon fairly early in the Gateshead epidemic, but it could have been given three weeks before. Then 6 of the 8 cases of post-inoculation poliomyelitis would not have been recorded as such, and at least three cases of post-inoculation paralysis would not have occurred. Now that poliomyelitis has become the most important acute infectious disease, intramuscular immunization should normally be suspended at once on the appearance of the first case of paralytic poliomyelitis in any year, in order to allow an assessment of the trend of prevalence of the disease. The earlier in the year the first case occurs, the more important it is to follow this course, for poliomyelitis in the spring presages a severe visitation.

Manufacturers of prophylactics differ in their advice regarding intramuscular injection. One firm recommends deep intramuscular injection above the insertion of the deltoid; another recommends that this should be given on the outer side of the thigh; and a third leaves it to the physician to choose the site. Certain considerations suggest that all intramuscular inoculations of prophylactic antigens should be given in the buttock or thigh, as is the custom in hospital. It seems that the amount of trauma in the muscle may exercise an effect on the severity and extent of post-inoculation paralysis. The smaller the muscle the greater the proportion of the whole muscle damaged by the injection of an irritant antigen. Local trauma will probably be more severe when an irritant antigen is injected into the deltoid muscle of an infant than when the same amount is injected into the gluteal or vastus muscles.

A further point concerns the observed tendency of the damage in the cord to spread locally so as to affect other muscles in the vicinity, to cross the mid-line so as to affect muscles innervated by the same segment of the cord and even to spread further. Now the fifth and sixth cervical segments of the spinal cord innervating the arms are continuous above with the segments supplying the diaphragm and below with those innervating the intercostal muscles. Thus respiratory paralysis in poliomyelitis is usually coupled with an arm paralysis. There is therefore at least a theoretical possibility that the possible spread of post-inoculation paralysis of the arm may involve the muscles of respiration, and that this has actually occurred seems to be demonstrated by three if not four of the cases reported by Geffen. Thirdly, it seems that the disability inflicted by an arm paralysis must be compared with that produced by paralysis of a corresponding degree and extent in the leg. Although there is room for controversy, it is felt that in modern conditions a paralysis of leg muscles which can be neutralized by modern orthopaedic appliances is to be preferred to a corresponding paralysis in the arm which cannot at present be compensated by appliances. These arguments indicate the election of the lower limb as the site for intramuscular injections.

It would, of course, be better still if all the prophylactic antigens were issued for use only after they had proved acceptable to the subcutaneous tissues, for proper subcutaneous administration would seem to avoid all the risk of inducing a subsequent paralysis. In the prophylactics incriminated in the matter under discussion, the presence of alum seems to emerge as the common factor. If immunizing antigens cannot be made suitable for subcutaneous administration, manufacturers would also be well advised to try to reduce the quantity of material to be injected, in order to minimize the amount of muscle trauma.

There is an obvious medico-legal aspect of the problem of post-inoculation poliomyelitis which concerns all who administer prophylactic antigens. In the interest of both patients and practitioners, it is particularly important that confirmed cases of poliomyelitis should be promptly notified in order that the medical officer of health may at once apprise and advise the practitioners of his area.

Summary

A number of cases of post-inoculation poliomyelitis personally encountered in Gateshead and district have been studied. It is concluded that there was no doubt of the increased risk to a child of developing a paralytic attack of poliomyelitis as a result of intramuscular immunizing injections at a time when poliomyelitis was prevalent.

A close look-out must now be maintained in every area for the appearance of poliomyelitis. Immediately the first confirmed case has been detected intramuscular immunization procedures should be halted for a short period so as to take stock of the situation.

Manufacturers of prophylactics should aim at the production of antigens which will be satisfactory in every way when given by subcutaneous injection.

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ACUTE APPENDICITIS IN INFANCY AND EARLY CHILDHOOD

BY

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Bailey and Love (1949) begin their section on appendicitis with these words: "Over 3,000 persons die annually from acute appendicitis in England and Wales alone. Many of them are in youth or the prime of life. Practically all these lives could be saved if an early diagnosis were made, and, at this stage, the comparatively simple operation of appendicectomy carried out. The importance of the subject cannot be overstated." Recent years have seen an improvement in the saving of lives, though not necessarily in early diagnosis.

In this paper are reviewed 115 consecutive unselected children whose appendices were removed. They were admitted to the wards of the Westminster Children's Hospital during 1950–2. Thirty-two suffered from "recurrent" appendicitis. The remainder had appendices which were unequivocally demonstrated to be the seat of acute inflammation. All were under 12 years old.

It is not proposed to deal in detail with those in the "recurrent" group or with those over 5, but to make special reference to the 28 cases under 5. It should be noted that in those cases which have been called "recurrent" there was evidence, either macroscopically or microscopically, of past inflammation in the appendix. Cases in which a normal appendix was removed, either through erroneous diagnosis or during the course of some other operative procedure, are not included.

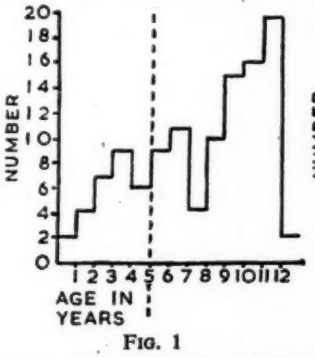

FIG. 1

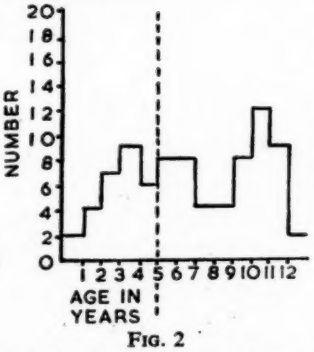

FIG. 2

FIG. 1.—Age incidence of whole series. FIG. 2.—Age incidence of non-recurrent cases.

Fig. 1 shows the incidence by age of all cases. Fig. 2 does not include "recurrent" cases. It is seen that quite a high proportion of cases occur under 5, and that "recurrent" appendicitis was not observed at all in this group, which will be subjected to further scrutiny; and the Table sets out those at each age who had complicated appendicitis and in whom there was an antecedent upper respiratory infection, and the main presenting symptoms. Complicated appendicitis is taken to mean the presence of general or local peritonitis, including abscess formation, on admission.

Age	No.	Complicated	Recent Upper Respiratory Infection	Presenting with D. or D. and V.
0–1 year ..	2	—	1	1
1 ,, ..	4	2	2	2
2 years ..	7	4	5	3
3 ,, ..	9	4	6	3
4 ,, ..	6	2	4	2
	28	12	18	11

Several facts now emerge. First, 28 (24%) cases occurred in children under 5, and among these the incidence of complicated appendicitis is high, being 43%; whereas in the older children the figure is only 18%. Secondly, a large number of children had diarrhoea, with or without vomiting as a presenting symptom, and in these there was a recent history of an upper respiratory infection. Such a history is often misleading, and judging from these cases it would seem that in the young child acute appendicitis is often missed.

The average duration of symptoms before admission to hospital was four days. Two typical case histories are given.

Case 1

A little girl aged 4 was seen one evening in the casualty department. Four days previously she had gone off her food, appeared listless, and complained of abdominal pain. She had recently recovered from a "sore throat," for which a course of penicillin injections was given, and was still having penicillin when her general symptoms appeared. Her temperature, which had fallen to normal limits, rose to 100–101° F. (37.8–38.3° C.) and the penicillin was therefore continued. She seemed to improve somewhat during the next four days but still complained of abdominal pain, and her bowels were opened several times, the motions being very loose. This state of affairs continued until she was brought to hospital.

On admission her temperature was 101° F. (38.3° C.), pulse 120, and she looked flushed and ill. On examination the abdomen was a little distended and did not move well with respiration. She was tender to palpation in the right iliac fossa and in the midline below the umbilicus, but owing to guarding nothing definite could be felt. On rectal examination, however, a tender mass could be felt high up on the right, and the finger of the glove was covered with mucus.

She was put to bed and kept under observation. By the next day her abdominal pain seemed less, and on careful examination the mass could also be felt through the abdominal wall. It was decided to treat her conservatively, and over the next three weeks the abscess gradually resolved. She was finally sent to convalescence and readmitted four months later, when a fibrotic and still slightly adherent appendix was removed.

Case 2

A boy aged 3 was admitted with a three-day history of abdominal pain, vomiting, and diarrhoea. At the onset he had started vomiting one evening after his meal. He was put to bed and later complained of abdominal pain, which woke him up. Early next morning he passed two very loose motions. On examination at that time he apparently had few physical signs beyond some tenderness across the lower abdomen. His temperature was 100° F. (37.8° C.) It was thought that he might have an enteritis, so a course of chloramphenicol was begun. His symptoms temporarily improved, but his temperature remained between 100 and 101° F. (37.8 and 38.3° C.). He had no further diarrhoea, but vomited twice the next day. His pain got no worse. The following day, however, he appeared much worse, the vomiting recurred, and his pulse rose to 130. The abdomen was by now distended and tense, and showed tenderness all over, especially below the umbilicus. He was immediately sent to hospital.

On admission his temperature was 102.4° F. (39.1° C.) and pulse 146. He appeared extremely ill with obvious peritonitis, the abdomen being tense, tender, and silent. At operation a spreading peritonitis was found with little or no attempt at localization, the cause being a gangrenous

appendix, which was removed. He was given aureomycin intravenously.

His convalescence was stormy and he had a further operation for the relief of small-bowel obstruction due to kinking from an adhesion. However, he was finally fit to go home nine weeks after his operation.

Treatment

Treatment has in no way differed from that now generally advised by all authorities. Immediate operation is carried out in all early acute cases. Those in whom an abscess has formed are treated conservatively unless spread demands drainage. The appendix is removed four to six months later. Those with peritonitis have had the remains of the appendix removed and the peritoneal cavity drained if the amount and character of the exudate warranted it. Drainage was needed in 9% of all the cases.

In one respect I find we differ from most other surgeons who have published series of similar cases—that is, in our use of Graham's incision, instead of McBurney's, as advocated by Mr. David Levi. We find it gives an extremely good exposure, is quick to make and close, and is easily extended if more room is required; also it does not imperil any nerves even if suppuration occurs.

In every recent series published the ultimate credit is given to the antibiotics. Certainly among our own patients there were several who would have undoubtedly died had it not been for these drugs—in particular aureomycin, which was given by intravenous drip. Doses of 100 mg. were given six-hourly, dissolved in 10 ml. of 1.95% leucine as supplied by the makers. Five to ten minutes were taken to inject the solution into the drip tubing to avoid undue pain and to minimize the danger of thrombosing the vein. Rapid injections, apart from quickly setting up an irritant thrombosis, cause such intense pain that even a comatose patient is aroused.

Wright *et al.* (1949) reported six cases of general peritonitis following ruptured appendicitis, all of which recovered with aureomycin. Olshaker *et al.* (1950), using the same drug, reported six similar successful cases aged between 4 and 8.

There were no deaths in this series, which, though the numbers are comparatively small, is encouraging.

A "spectacular" drop in mortality in the United States was observed by Slattery *et al.* (1950) even for the years during the war—from 14,113 in 1939 to 5,285 in 1946. This they attribute, amongst other factors, to the use of antibiotics and the principle of non-intervention in abscesses. Weiss (1950) reckoned that the total mortality in and around New Orleans had fallen from 15.2 to 2.9 per 100,000 in the last decade.

Pathology

We found that most cases of acute appendicitis in younger children were catarrhal in origin rather than obstructive. I have no records of some of the earlier cases, but in all those which were examined obstruction by faecalith or stricture was the exception. In the older children faecaliths were common.

The initial site of inflammation is in the lymphoid tissue of the wall—tissue which is far more abundant in youth, and which, like the mesenteric glands, often takes part in infection elsewhere. As already mentioned, over 60% of these young children give a history of recent tonsillitis, otitis, or a "cold." Babcock (1944) stated that "infections that produce general lymphoid hyperplasia often precede appendicitis." Scott and Ware (1945) denied this, but it seems common experience, in this country at any rate, that upper respiratory tract infections are frequently forerunners of appendicitis.

In addition, it must be realized that the margin of safety in the young is small. A thin-walled appendix containing a mass of lymphoid tissue through which infection spreads easily, and a small ineffective omentum, contribute to early perforation and wide dissemination of infection.

Discussion

Most authorities seem generally agreed in several points concerning this condition in childhood. First, acute appendicitis is not common in children under 5. Under 3 it is "rare" or "very uncommon." Reyes and Pascual (1950), reporting a series of 50 cases, found the youngest to be 6. Secondly, the diagnosis in early childhood is difficult. Thirdly, the mortality is high. The second of these points is undoubtedly true, but for the others there seems less justification at the present time.

Of our 82 patients, 28 (34%) were under 5, an incidence which cannot be regarded as uncommon. Abel and Allen (1950) reviewed 1,165 cases treated at the Bellevue Hospital, New York, and found that 165 were under 5. Morton and Kilby (1950) found an incidence of 20% in 100 cases at Newark, N.J.

Packard and McLauthlin (1951), reviewing 280 cases at the Denver Children's Hospital during the five-year period 1945–50, found that the average age of patients with peritonitis was 4.8 years. For those with simple appendicitis it was 8.6. Of their patients, 25% were 4 or under, and of this group 60% had local or diffuse peritonitis on admission. The only death among these was in a 3-year-old child with a ten-days history.

In searching for some explanation there would appear to be three main causes. First, the difficulties in diagnosis already referred to; secondly, the practitioner is often loath to diagnose acute appendicitis at this age, or thinks of some other condition first because he has been taught that it is uncommon. Such phrases as, "This child seems rather young for an appendix," or, "Could this be appendicitis at this age?" are often encountered in letters accompanying the patient to hospital. They betray the diagnosis as being late, and even an afterthought. Lastly, I believe the picture of appendicitis at this age to be changing: not because of any alteration in the disease itself but because of the widespread, and in some cases indiscriminate, use of antibiotics.

Difficulties in Diagnosis.—The four earliest signs are pyrexia, abdominal pain, vomiting, and local tenderness. Any of these may predominate, any may be absent, and any may be associated with one other symptom which is uncommon in the older patients—namely, diarrhoea.

Temperature and Pulse.—In a young child very little constitutional upset is enough to produce a considerable rise in temperature and pulse. It is often said that a high temperature associated with abdominal pain is rather against appendicitis and in favour of pyelitis. This is dangerously untrue, especially if a thorough examination of the urine is neglected. Half our patients had temperatures of over 101° F. (38.3° C.) and a quarter over 102° F. (38.9° C.). The pulse is proportionately raised—a ratio of 12 to each 1° F. (0.55° C.) rather than 10. The rate is not of such importance as a steady rise.

Pain.—This is notoriously difficult to assess in the very young. It is usually colicky or cramp-like and initially comes in waves, causing crying and screaming attacks with the knees drawn up. After a time it becomes continuous and the child lies characteristically curled up. Localization is also poor, and if the patient is of an age to understand the question he usually puts a hand on the umbilicus. Tenderness, on the other hand, is confined to the right iliac fossa, unless perforation has already occurred. In the early case a difference in "tension" of the two sides of the abdominal wall is more easily appreciated by very light palpation with the tips of the fingers. Strang (1950) recommends examination of the abdomen from behind with both hands while the child is held in the mother's arms in the natural nursing position. In this way we avoid a crying, frightened child in whom abdominal palpation is impossible. In other cases stealthy examination of the abdomen with the hand under the bedclothes may be better. The disappearance of "abdominal" breathing and its replacement by "thoracic" respiration also occurs surprisingly early on, and must be

carefully looked for. The most dangerous aspect of pain is its disappearance when perforation occurs. The child, after what may have seemed a trivial abdominal disturbance, appears well for several hours. He may even show a desire for food or fall quietly asleep. The sinister sequence of a steadily increasing pulse and abdominal distension is all too early missed after the parents' and one's own conscience has been reassured. The following morning may be already too late. It is surprising not only how well many such patients appear at this stage but also how rapidly and alarmingly their condition may suddenly deteriorate.

Vomiting and Nausea.—These, with pain, form possibly the commonest manner in which the condition presents. But again a note of warning should be sounded. Reliance on the old axiom "Pain precedes vomiting" can easily mislead; for in many cases the sequence is reversed. Both may be absent.

Diarrhoea.—This may be a cardinal sign, and much more often than is generally supposed it is so. It may occur with or without vomiting. A diagnosis of enteritis or food-poisoning is fatally easy. How many of us have not had the humiliation of referring an unsuspected acute appendicitis to a fever hospital? Diarrhoea is often the first presenting sign in infants; the stool is very loose, often containing mucus, but never blood. It is due to the proximity of the appendix to the sigmoid or upper rectum. The child's pelvis is very small compared with the length and size of the appendix, and such contiguity may be demonstrated at operation. The caecum may be similarly irritated. Spurious diarrhoea coming on two or three days after the onset of pain, and consisting of small amounts of faeces-stained mucus, is pathognomonic of an appendix abscess. Rectal examination will reveal the mass. Auscultation, while it may show normal or near normal amounts of peristalsis, will not disclose the excited hubbub of the enteritic. Silence means ileus and peritonitis.

The High Appendix.—It is often loosely stated that in children the appendix lies high in the abdomen; sometimes under the liver. This may well be true, and every surgeon at one time or another has experienced confusion in diagnosis and difficulty at operation in removing such an abnormally placed organ. But the condition is a true abnormality. It is a defect in the last stage of the rotation of the gut. It is not common. Only two children in this series showed it, and in only one was it of a degree to cause trouble at operation.

It has been said that the surest sign of appendicitis is tenderness over the appendix, and the proper and usual place for the appendix is just above the brim of the pelvis in the right iliac fossa.

Finally, a point which I believe to be often responsible for the diagnosis being missed. If a child has sought medical aid because of inflammation remote from the peritoneal cavity the almost invariable treatment now afforded is an antibiotic, usually a sulphonamide or penicillin, although chloramphenicol is beginning to gain ground in popularity. The most dangerous complication of these chemicals is the masking of any extension of such inflammation and especially of abscess formation.

Should a metastatic lesion now develop, the classical signs are absent. There is little if any increase in constitutional signs. The appendix can perforate in comparative quietude and large quantities of pus collect without notice. This becomes doubly dangerous in the inarticulate young. As a result the picture of appendicitis is very different from that which used to be taught and expected in practice.

In conclusion it may be said that the only real safeguard is unceasing vigilance—a thorough examination if, and when, any abdominal symptoms develop, which may mean repeated visits even though this is onerous to a busy man.

Professor Aird (1949) has said that the old saying "Never wake a child at night to have an operation" is not dependable, and by the same token should be mentioned Mr. Levi's maxim that "if abdominal pain in a child, associated with vomiting, lasts continuously for more than six hours and is unrelieved by an enema, he should be seen by a surgeon." Some may dismiss these as "rules of thumb." They may be—but they can be most helpful in times of doubt.

This renewed anxiety concerning the late diagnosis of these little children is not parochial. Packard and McLauthlin (1951) stated that "slower recognition of the diagnosis seems the most important factor in the markedly increased incidence of abscess and peritonitis in the infant and young child," and that "the high incidence of appendicitis with peritonitis in the very young child because of delay in diagnosis presents a challenge."

Riker (1950) out of 136 cases found 56 with rupture on admission: two died. He gives no figure for those in infancy, but states that there was "a high incidence of perforation in early childhood." Hawk *et al.* (1950) had 139 cases under 10. The youngest was 5 months old, and six out of eight children under 2 had peritonitis. There were no deaths in this series. In Reyes and Pascual's (1950) series 68% of cases under 10 had local or diffuse peritonitis. In Abel and Allen's (1950) 1,165 cases there was a 10% mortality in 165 cases under 5, as opposed to 2.9% in the remaining thousand. The majority of deaths occurred in the years before the war. Howard Williams (1947), of Melbourne, said of this condition, "Early diagnosis . . . will be established only by better clinical training of the student, family physician, and paediatrician." It would seem that the lesson has not yet been learnt.

Summary

A review of 115 cases of appendicitis is given; 82 had acute appendicitis. Special reference is made to those aged under 5. The high incidence (43%) of complicated appendicitis in this age group gives cause for concern.

Some difficulties in diagnosis are discussed and a plea is made for earlier diagnosis. It is suggested that the widespread use of antibiotics is changing the picture of appendicitis in the young.

I wish to thank Mr. David Levi and Mr. G. H. Macnab, of the Westminster Children's Hospital, for their helpful advice and criticism.

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Accident Prevention and First Aid in the Home, a 24-page illustrated booklet published by Messrs. E. & S. Livingstone, Edinburgh (price 1s. 6d.), indicates the commoner precautions that should be taken to prevent accidents in the home, and advises on the measures to be taken and those to be avoided if accidents should occur. Each point is driven home with a suitable illustration. The booklet is intended for mothers and those having the care of small children. It has been compiled by the surgical staff of the Royal Hospital for Sick Children, Edinburgh, and profits from its sale are to be devoted to the treatment of children brought to that hospital as a result of home accidents.

THE PRINCIPLES AND PRACTICE OF YAWS CONTROL

BY

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With the use of such a powerful and satisfactory drug as procaine penicillin in aluminium monostearate (P.A.M.) in the mass treatment of yaws, it may be useful to consider the principles and practice of yaws control based upon present knowledge. The realization of these possibilities is largely due to the work of the national and international staffs carrying out the W.H.O./U.N.I.C.E.F. Treponemal-disease Control Programmes.

The Principles of Yaws Control

I. Decision to Undertake the Anti-Yaws Campaign

This indicates that those in executive positions realize or have been convinced of the necessity for such a campaign. The purpose of the campaign will be the eradication of yaws from the community, not merely its reduction to some ill-defined low endemic level. The technique of the campaign must be adequate, scientifically sound, and economical. The campaign is a public health measure applied to the community and not a curative measure applied to the individual.

II. Decision to Undertake Activities After the Campaign Itself has Subsided

Experience in many parts of the world (Harding, 1949) has shown that this is, in practice, as important as the planning of the campaign itself if lasting benefit is to result. Failure to undertake post-campaign measures has often led to a return of the yaws incidence to the level preceding the control measures.

III. Planning and Execution of the Campaign Itself

These have become matters of skilful organization and careful supervision.

(i) A complete census of the whole population is made by the civil administrative authorities.

(ii) A medical survey of the whole population is then carried out so that all patients with infectious yaws and all persons likely to develop infectious yaws, especially during the next year, are recognized. This last group includes (1) all who have not yet had yaws but who have been in contact with infectious patients either in the household, village, school, or more remotely—the importance of these regions of contact varies with age (Soetopo and Wasito, 1953); and (2) all those in the latent secondary stage. The latent secondary stage is that in which a patient, who has had yaws, has no clinical manifestations at the time, has a positive Wassermann, Kahn, and other similar serological reaction in his serum, and has had no tertiary destructive lesions. At present this stage can be defined but not directly recognized.

(iii) Adequate treatment is given at the time of recognition on the survey to all patients in the above categories. A single intramuscular injection that will result in serological reversal is ideal.

If it once be recognized that it is a public health measure that is being carried out, there is no reason why, as a separate but concurrent measure, patients with other lesions due to yaws, or even other diseases, should not be treated. Such action must not jeopardize the success of the preventive measure that is planned to treat all infectious and potentially infectious patients so that the source of infection will be eradicated and thus transmission stopped. A wider range of treatment, especially in areas where other treatment facilities are not readily available, may help to gain the co-operation of the people and thus facilitate the work of the campaign. In all large campaigns there might be certain areas where investigations are carried out with the purpose of improving the effectiveness of the campaign itself.

IV. Post-campaign Activities

These comprise: (i) At the very start of the campaign the establishment of rural dispensaries or small treatment centres to be staffed by trained medical auxiliaries under medical supervision. At these centres free treatment would be available for all yaws patients and perhaps some other diseases. Members of the staff, after the mass treatment, would make tours of inspection of the related villages to recognize and treat infectious yaws; cases of other diseases would probably be referred to the treatment centre. As the breadth of the work expands and more diseases are brought under control the therapeutic activities of these centres would become less important and the preventive ones more important, so that they may more appropriately be called "prevention centres." "Health centres" may be preferred by some, but a rather special meaning has become attached to these larger, more urban, and more complicated establishments, while "rural centres" may be suggested by others, but no non-urban population likes to be called "rural."

(ii) Measures to recognize and treat, and thus prevent, the reintroduction of the infection into the population from other areas, and also recognize and treat any patients who have developed infectious lesions since the mass treatment. These measures may involve some form of rapid survey of the whole population and treatment at three- to six-monthly or longer intervals and especially itinerant medical auxiliaries. There might well come a time when contacts of the few cases of yaws that are found would be sought.

(iii) The undertaking of further control measures against the next most important disease for which there is effective treatment available which can be given by the staff of the prevention centre. The high incidence of an endemic disease before a campaign may make its effective treatment numerically impossible at a small rural treatment centre. However, after effective mass treatment it should be easily dealt with at a prevention centre.

The need for post-campaign activities was first realized and demonstrated by Harding (1949) in Sierra Leone, but these were not fully described in his paper as published.

In his few reprints he added a typescript insertion. With the permission of his widow, who worked with him in the field, this is being published here. The addition by the late Dr. R. D. Harding follows the "Conclusion" on page 365 of his article:

"Though not strictly connected with yaws, the possibilities of carrying out other medical activities in rural areas in conjunction with a yaws campaign may be briefly outlined by indicating ancillary work actually done during 1946. By the end of that year seven dispensaries had been designed and their attendants trained to treat most ailments and the diseases endemic in their localities as well as sleeping sickness and yaws, while seven less ambitious dispensaries were designed to treat only sleeping sickness, yaws, wounds, ulcers, scabies, malaria, bilharzia, ankylostomiasis, ascariasis, and amoebic dysentery. Two maternity centres were built in areas where the chiefs and people were favourably disposed to this innovation and suitable girls were available for training as midwives. (The lady doctor and sisters of Segbwema Methodist Mission Hospital, situated in the vicinity, very kindly undertook their training.) On the health side, the nuclei of two new chiefdom headquarters villages were laid out and their construction supervised, to replace the old villages consisting of dirty and crowded huddles of huts. Wells were dug and springs impounded to provide an alternative water supply to the foul puddles previously used. Citrus, guava, pawpaw, and other fruit trees provided by the Agricultural De-

partment were planted round the dispensaries in the hope that in course of time the villagers would learn to appreciate these fruits and cultivate them themselves.

"During the year 40,250 cases of all kinds were treated at the yaws dispensaries. Of these 10,400 were yaws, 1,530 sleeping sickness, 700 bilharzia, 580 hookworm, 1,760 ascaris, and 660 amoebic dysentery. There were 260 confinements in the wards of the maternity centres (one of which only opened in October), and there were 3,300 antenatal and 4,700 baby clinic attendances. 74,000 people were examined by touring teams. The entire European staff comprised three medical officers for half the year and two for the remainder, but one of these was engaged for nearly the whole year on a special trypanosomiasis investigation. The overall cost, including salaries, equipment, buildings, transport, etc., but possibly excluding drugs and dressings for diseases other than sleeping sickness and yaws, was under £10,000. These activities would not have been possible without the confidence which the successful treatment of sleeping sickness and yaws had engendered, and the close contact between populace and staff arising from the mobile character of the campaign.

"The possibility of mass treatment or control of other endemic diseases by mobile teams was carefully considered, particularly gonorrhoea and bilharzia. Gonorrhoea is extremely prevalent, but apart from difficulties of accurate diagnosis, the prohibitive cost of penicillin on the one hand and the inadvisability of handing out sulphonamide tablets for patients to take home on the other made the project of mass attack on this disease quite impracticable; the end-result of an attempt at mass treatment would almost certainly have been a local trade in sulphonamides, demoralization of attendants, and the development of resistant strains of gonococci, without any marked or lasting lowering of the incidence of the disease. A study of the local epidemiology of bilharzia, which in one locality affected 75% of the population, would have been undertaken if the staff position had allowed, but it would no doubt have taken several years to evolve suitable methods of control over a wide region, and the money and personnel required would greatly exceed that necessary for controlling sleeping sickness or yaws over the same area. It therefore seemed better to concentrate available resources on those improvements in general sanitation and midwifery which were possible in the immediate vicinity of the dispensaries, together with the treatment there of those endemic diseases readily diagnosable and curable by attendants trained for the purpose and proficient in the use of the microscope and the syringe."

This principle, that an anti-yaws campaign must be made the means of improving rural health services, was more recently stressed at the First International Symposium on Yaws Control in Bangkok in March, 1952, by Troupin *et al.* (1953).

The Practice of Yaws Control

The application of the above principles may be briefly discussed under the same headings.

I. Decision to Undertake the Anti-Yaws Campaign

In many countries in the past, it is possible that the numerical, medical, or economic importance of yaws may not have been fully realized at executive headquarters, since it is a disease of the more remote rural areas. It may also have been realized that, although a few injections or arsenical or bismuth preparations might work temporary wonders, their effect as a rapid public health measure was poor. However, in some areas in the past relatively casual but widespread treatment with bismuth has, after some years, apparently resulted in a very considerable numerical decrease in yaws. Again, the populations of yaws endemic areas are usually undeveloped and have often not understood the importance of the disease to themselves and the need for more continued treatment than might appear obvious to them. It will be generally agreed that in all countries in which yaws is endemic there also occur several other diseases more important as causes of sickness and death. These may include malnutrition, tuberculosis, malaria, and schistosomiasis. All these factors militate against the initiation of anti-yaws campaigns. With the realization of the immediate effects and ultimate possibilities of successful yaws control by mass treatment with P.A.M., there is much greater encouragement to undertake these measures.

II. Decision to Undertake Post-campaign Activities

Unless the vital importance of these activities is realized at the start of the anti-yaws campaign they will not be included in the planning. Thus the purpose of the campaign will be lowered, with loss of inspiration to those engaged in it. Even if these post-campaign activities are later undertaken continuity may be lost. The interest and confidence of workers and populations may be weakened and ultimate success gravely jeopardized. Although the immediate purpose of the anti-yaws campaign is the eradication of yaws the ultimate purpose of the campaign must be the gradual but steady and secure improvement of the rural health services. When one step is approaching successful completion the next in importance that is within the financial resources of the community is started; thus each improvement gained is maintained with certainty.

III. Planning and Execution of the Campaign Itself

(i) *Preparation of the Census.*—This has now become a routine civil administrative process of well-established practice.

(ii) *Survey.*—Unless a survey is carried out there is no way of assessing either the need for the campaign or its success. It is, of course, upon the findings of the survey that the mass treatment is based; all the population must be examined so that all infectious and potentially infectious yaws patients can be treated. Research may reveal some technique, such as an intradermal test with specific antigens, which will make possible the recognition of the latent secondary stage. As anti-yaws mass therapy becomes better established it may be practicable to search for other diseases in the same survey.

In countries where the rural population lives mostly in large villages or small villages close together, surveys can best be made by arranging for the authorities concerned to have the inhabitants gather at a suitable place at a certain time. In Indonesia, where this is done, it has been shown that one simply trained local medical auxiliary can examine over 750 persons each week. Those suffering from yaws are directed to a near-by established clinic (Soetopo and Wasito, 1953).

Where, however, the villages are small and scattered or where the population live in widely dispersed houses this method is impracticable and house-to-house visits must be made. Guimarães (1953), of the Instituto Oswaldo Cruz, when working in the Baixade Fluminense, near Rio de Janeiro, used local persons, chosen for their intelligence and initiative, to make the house-to-house survey and to refer patients to the yaws treatment centre. This employment was part-time, and payment was made according to the number of patients found. However, the payment per patient was raised as the campaign progressed in an area and the number of patients greatly decreased. Since these persons relied largely upon their usual occupations for their living they naturally made their house-to-house inspections "after hours," which is the time most country folk are at home. Only local people could have found the houses. Perhaps in village communities in which the incidence of yaws is low house-to-house surveys would be the method of choice. The co-operation of the population and their leaders is essential throughout the campaign. This is possible only if the purpose of the campaign is understood and the campaign desired. This has been shown in combating African trypanosomiasis in places where the population has learnt its deadly nature. It is equally important that those engaged in the campaign itself should understand the outlook of the population and that there should be mutual sympathy.

(iii) *Treatment.*—This, ideally, would be a single intramuscular injection of a cheap, effective, and non-toxic drug. This would go far to win the co-operation of the population. There must be as little trespass upon the time of the population as possible. Their occupations may be mainly agricultural, but at many seasons of the year they will have

little time to spare to attend survey-treatment gatherings. In Yugoslavia mass treatment against epidemic syphilis is available in villages at any reasonable time throughout the day, so that the patients' activities are interfered with as little as possible.

The Committee on Venereal Diseases and Treponematosis, at the 4th session in London, July/August, 1952, recommended that "in mass campaigns against non-venereal treponematoses the minimal dosage for early infectious lesions in adults be no less than 1.2 mega units of P.A.M. [of approved standard] and proportionally less for children; that this dose be given in one injection and that the preventive (or 'abortive') dose for contacts be no less than one-half of that used in the early infectious stages of the established disease."

The staff of the prevention centre should be carefully selected from the local people and suitably trained under the same conditions of buildings, equipment, and supplies as they will have in the final appointment. This employment of local people—under, of course, some medical supervision—has in many countries been completely satisfactory. It is economical, and as nearly as possible ensures a contented staff. Their influence for good health can far exceed that due to their official duties.

Until some means of detecting the latent secondary stage has been evolved, one of three expedients might be used. Treatment might be given to: (*a*) all who have had active secondary lesions during the previous five years (Saunders, 1937); (*b*) all of the population under 18–20 years of age, which will include 80–90% of persons likely to suffer infectious relapses; (*c*) all children at schools and in the 2–6-year age group who have yaws or have a history of having had yaws (these may comprise 80% of the scholars in some endemic areas). This action would cover many "contacts" of the disease. Contacts outside these ranges would not be very important.

IV. Post-campaign Activities

(i) The establishment of rural dispensaries suitably located to serve the population—the prevention centres already referred to—may well be regarded as the most important achievement of the anti-yaws campaign. Perhaps it would not be extravagant to say that their establishment during the campaign is the first step, to which the campaign itself was only the way. The importance of these rural dispensaries with itinerant staff, which was clearly demonstrated by Harding (1949), cannot be overemphasized, and until their importance is realized much money and effort in anti-yaws work may still be wasted. Of course, if other established static units are already present they would become the centre of the development.

(ii) Prevention of the reintroduction of the disease into an area in which yaws had been controlled could best be achieved by extending the range of anti-yaws campaigns as widely as necessary. It should be regarded as absolutely essential to the success of any mass-treatment campaign that effective case searching and treatment facilities remain in the field, so that the few cases which are certain to occur during the following year may be dealt with. There is not, and probably will never be, any drug which in mass use will produce cure in all patients.

(iii) The carrying out of further control measures against other diseases that can be diagnosed and treated by the staff is the logical sequence of the stabilization of the campaign results and the rural dispensaries. All through these progressive achievements the education of the population in preventive matters would be taking place, even without the intentional efforts that would be made at every opportunity. There is an urgent need for the discovery of some educational technique which could be applied to health and other problems among undeveloped people. It is probable that the purpose of such a technique would be to create in the people a strong desire for the improvement that is intended. The late Dr. Harding's notes, published above, show what can be done and what should be planned for.

Summary

For a long time yet the sequence of census, survey, and treatment of yaws will be required. Procaine penicillin or some other depot preparation will, with difficulty, be improved upon. The importance of recognizing cases in the latent secondary stage of the infection must be emphasized; some way to doing this is urgently needed.

An anti-yaws campaign is only a means to an end, and that end is the gradual and stable development of improved rural health services. This alone can justify the efforts required to carry out an effective anti-yaws campaign. Such a campaign, in areas where yaws is endemic, is probably the best first step in the improvement of rural health services.

The work of the World Health Organization and the United Nations International Children's Emergency Fund in assisting treponematosis control work in various countries is of great importance, and is an encouragement for the future. Reynolds *et al.* (1951) discuss the ways this help can be most effectively applied.

Professor G. Macdonald, of the London School of Hygiene and Tropical Medicine, saw this article before publication and has made the following pertinent comments:

"I am convinced that the general principle is sound. The extension of such work depends on what is wanted. If what is wanted is to start a rural public health service, there is no doubt that the best way of doing so is through measures which are immediately obvious to the population as beneficial, and of course yaws is one of the more prominent examples. Credit earned by this such work could be used to persuade people not to accept other obviously less useful work. If I were starting such a scheme I would want a curative measure, such as yaws treatment of this nature, and also an environmental measure. Quite the best example of the latter is the application of residual insecticides in houses, which is appreciated at once for the effect on fleas and flies and later for that on malaria. I would therefore start with a yaws campaign and a residual insecticide campaign as initial steps towards a rural health centre service which undertook environmental and curative work. The approach, in the paper, to the curative side of it seems ideal."

This combined attack is being carried out by W.H.O. in Liberia.

I am deeply indebted to Dr. Kodijat and his staff in Indonesia, to Dr. F. Nery Guimarães, and to those whom I met of the Division of Sanitary Organization of the National Department of Health concerned with yaws control in Brazil, for information about their work.

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According to a report of the Committee on Child Health of the Scottish Health Services Council, only about 50% of mothers attend with their infants where child welfare clinics are provided. This is a matter of concern, although the report records a great improvement in child health in recent years. The importance of instruction in breast feeding and mothercraft is stressed. Every effort should be made to underline the value of immunization against certain infectious diseases. Recommendations are made regarding the management of premature infants: the report considers that breast-milk should be available to all infants in hospital, and that milk banks should be established where necessary. The report (*Child Health*) is published by the Department of Health for Scotland and is available at H.M. Stationery Office, price 9d.

EFFECT OF LARGE DOSES OF HISTAMINE ON GASTRIC SECRETION OF HCl

AN AUGMENTED HISTAMINE TEST

BY

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In the routine histamine test of gastric secretion the dose of histamine advised has been determined arbitrarily as being generally sufficient to provoke an acid response and generally free from liability to cause untoward symptoms. It is thus a compromise, and fails to take account of individual variations in susceptibility. This defect can be overcome by utilizing the group of synthetic drugs known as the antihistaminics.

These compounds have been shown to antagonize all histamine effects save that on gastric secretion. This interesting anomaly has been well demonstrated by the work of Halpern (1948). He has shown that, although guinea-pigs could be protected against the systemic effects of as much as 1,500 lethal doses of histamine, many animals died within a day or two as a result of gastric perforation.

The purpose of this paper is to describe the parietal cell response in man to large doses of histamine, the systemic effects of the drug being prevented by the use of an antihistamine. It will be shown that in this way it is possible to give a maximum stimulus to the parietal cells. An augmented histamine test of gastric secretion, based on this principle of maximum stimulation, is described and an analysis made of the results of 148 such tests performed on normal subjects and on patients with peptic ulcer.

Secretion of HCl after Increasing Doses of Histamine

Dosage.—Throughout this investigation histamine has been given subcutaneously as histamine acid phosphate in multiples of the usual body-weight (B.W.) dose of 0.1 mg. per 10 kg. body weight. Mepyramine hydrogen maleate ("anthisan") was chosen as the antihistamine. In a series of preliminary experiments it was found that, in order to protect the patient against the systemic effects of histamine, each body-weight dose of histamine had to be covered by 1 ml. of mepyramine (25 mg.). It was also found that the antihistamine should be given intramuscularly 30 minutes before giving the histamine injection. Thus, a patient about to be given four B.W. doses of histamine would have an intramuscular injection of 4 ml. of mepyramine 30 minutes previously.

Secretion Studies.—Secretion tests were begun at 9 a.m. following a 12-hour fast. A constant size of stomach-tube, having multiple perforations at its tip, was used throughout. The fasting juice was first aspirated by syringe, the position of the patient and the position of the tube being altered until the "residual pool" of gastric juice had been tapped. This achieved, the tube was fixed to the side of the face and the patient made comfortable in this position—usually reclining on the left side. Subsequent collection of gastric juice was made by continuous aspiration, using the suction provided by an electric pump. The spontaneous secretion was withdrawn for a control period of 45 minutes before giving mepyramine, and thereafter aspiration was continued for 30 minutes until the histamine injection was made. The volume of the gastric juice withdrawn in the 45-minute period after histamine was measured and the titratable free hydrochloric acid estimated. The weight of HCl secreted in this time was then calculated and expressed in milligrams of HCl. All saliva was expectorated during these tests.

Effects of Increasing Dosage of Histamine.—With these standard conditions, one, two, three, or more B.W. doses of histamine covered by the requisite amount of antihistamine were given to each subject on successive days. The order in which the different doses was given was varied in each subject. This series of experiments was made on five "normal" males (hernia cases without history of dyspepsia) and on five male patients with clinical and radiological evidence of duodenal ulcer. In all, 77 separate secretion tests were made. The largest single injection of histamine given was the equivalent of 12 B.W. doses; thus one ulcer patient was given 6.8 mg. and one normal subject 7.1 mg. without untoward effects. Headache and flushing were not more severe after large doses of histamine than after the usual single B.W. dose uncovered by antihistamine. The latter often induced drowsiness, which enabled the subjects to endure more readily a trying succession of secretion tests.

Results.—The weights of HCl secreted in 45 minutes in response to various doses of histamine have been plotted as ordinates on a graph, with the dose of histamine along the abscissa: in both groups of patients an S-shaped curve was produced (Figs. 1 and 2). It will be seen that maximum HCl output follows the giving of four B.W. doses of histamine and that any further increase in histamine dosage is not followed by appreciable change in acid output. It seems probable that, with increasing doses of histamine, an increasing number of parietal cells are stimulated until the entire parietal cell population is functioning. This is in agreement with the findings of Card (1952).

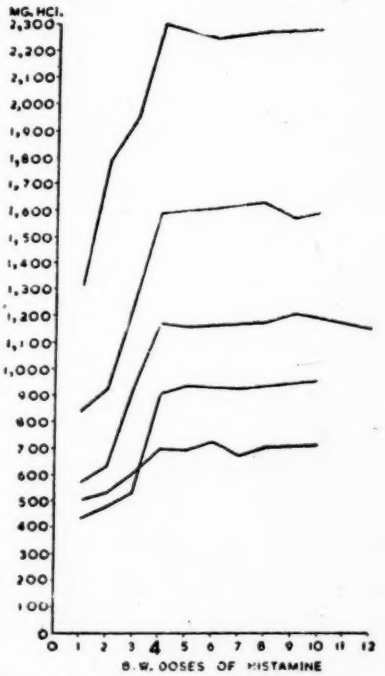

FIG. 1.—Dose-response curves in five cases of duodenal ulcer.

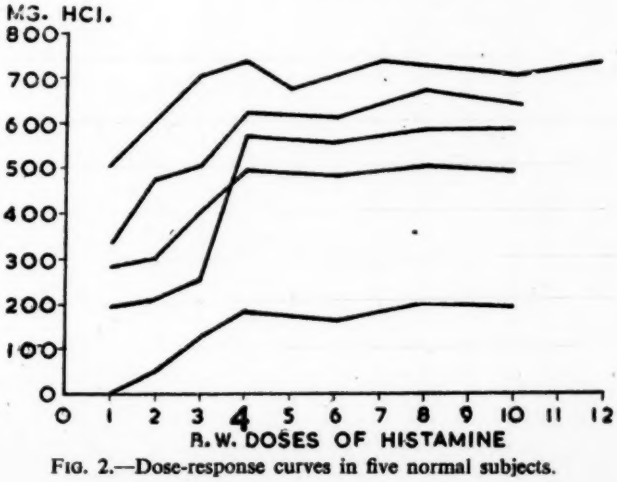

FIG. 2.—Dose-response curves in five normal subjects.

Duration of Maximum HCl Secretion after Four Body-weight Doses of Histamine

The following observations were made to determine the duration of the secretory response to large doses of histamine with a view to standardizing an augmented histamine test.

Eight male patients with duodenal ulcer were selected for study. Each patient was given a single test in which the subcutaneous administration of four B.W. doses of histamine was preceded by an intramuscular injection of 4 ml. of mepyramine. The juice was again collected by continuous suction, but the collecting vessel was changed every five minutes for a period of one hour. The weight of HCl secreted in each five-minute period was expressed in milligrams of HCl.

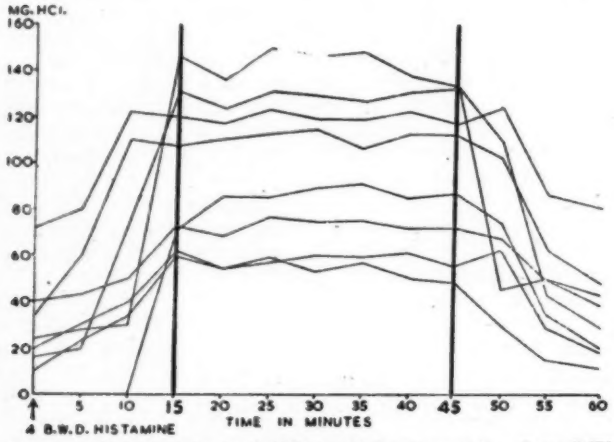

FIG. 3.—Gastric output of HCl (mg.) in response to four B.W. doses of histamine. Continuous aspiration—five-minute specimens from eight patients.

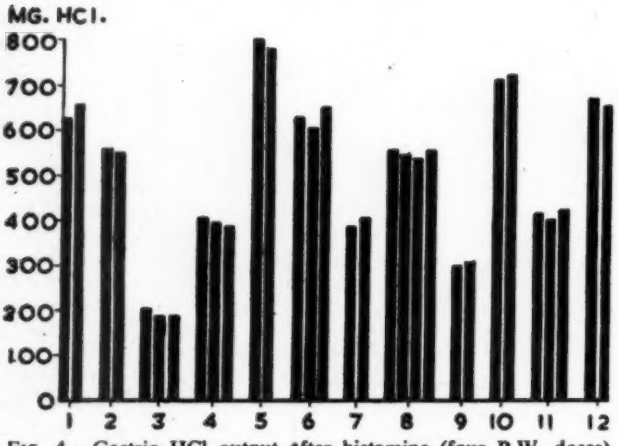

FIG. 4.—Gastric HCl output after histamine (four B.W. doses). Repeated estimations in 12 patients.

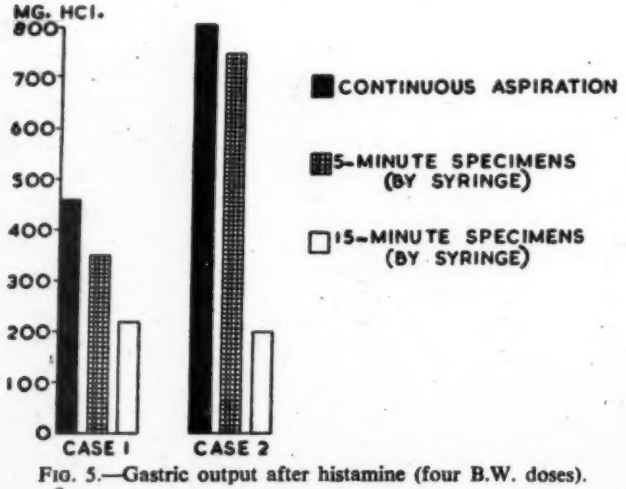

FIG. 5.—Gastric output after histamine (four B.W. doses).

In all cases maximum output was reached in about 10–15 minutes and persisted for the next 30–35 minutes (Fig. 3). The best measure of output, therefore, is based on the secretion during the half-hour period from 15 to 45 minutes after administration of histamine.

Adopting this half-hour period of continuous aspiration, each of 12 patients was given two or more tests on successive days. The consistency of consecutive estimations is shown in Fig. 4. The error occurring between separate tests was about 5%.

That it is essential to collect the gastric juice by continuous aspiration has been shown by a simple experiment in which the histamine test was repeated on three successive days on each of two patients. The method of aspiration was the only variable factor in the three tests: continuous aspiration was used on the first day, syringe removal at five-minute-intervals on the second day, and syringe removal at 15-minute intervals on the third day. It will be seen that the "maximum" HCl output of the stomach appears to fall when interval aspiration is employed (Fig. 5). This fall is due to the reduction in the volume of juice aspirated from the stomach, a considerable amount having been lost through the pylorus in the intervals between aspiration.

The Augmented Histamine Test

The test to be described is based on the conclusions reached in the foregoing studies. It provides two single results expressed in milligrams of HCl. The first figure indicates the basal secretion, and the second gives an expression of maximum parietal cell activity. The test is made as follows:

(1) The test is preceded by a 12-hour fast.

(2) A No. 9 stomach tube is introduced into the stomach and the fasting juice aspirated by means of a 50-ml. syringe. It is essential to alter the position both of the tube and of the patient until the tip of the tube reaches the most dependent part of the stomach and permits aspiration of the residual pool of fluid. This position of the tube is now maintained by fixing it to the side of the face and by insisting that the patient does not alter his posture until completion of the test. This will usually mean that he will lie comfortably on his left side.

(3) The spontaneously secreted gastric juice is now collected for a period of 45 minutes and the basal secretion expressed in milligrams of HCl produced in this time interval.

(4) 4 ml. of mepyramine is now given by intramuscular injection.

(5) The gastric juice is aspirated for the next 30 minutes and is discarded.

(6) A subcutaneous injection of a 4 B.W. dose of histamine acid phosphate is now made.

(7) The histamine-provoked secretion is continuously aspirated and the volume secreted in the half-hour from 15 to 45 minutes after injection is measured and its titratable free HCl estimated. The weight of HCl produced in this 30-minute period is the figure expressing the maximum parietal cell response.

This test of gastric secretion has certain advantages over other gastric-function tests. It is simple to do and lasts only two hours. The systemic effects following the administration of a large dose of histamine are prevented and the main subjective sensation is the drowsiness due to the antihistamine. More than 200 such tests have now been made in this unit without incident. It provides two figures—one expressing basal secretion and one maximum secretion of HCl.

Analysis of Results of 148 Augmented Histamine Tests

The histamine test described, unlike other tests of gastric secretory function, has been shown to impose a maximum load on the secretory cells whose function it is designed to test. Furthermore, the consistency of consecutive estimations has been demonstrated. In an attempt to establish standards of normality for the test and note deviations from these

standards in patients with peptic ulcer, 148 subjects have been examined. This group comprises 25 normal subjects, 103 duodenal ulcer cases, and 20 patients with gastric ulcer. All were males. The normal group consisted of patients awaiting operation for hernia; in none was there a history of dyspepsia and none were febrile. The diagnosis in the ulcer patients was confirmed at operation in every case.

Results.—In the normal group the average basal output of HCl was 70 mg. and the average maximum output 422 mg.; in patients with duodenal ulcer the basal output averaged 265 mg. and the maximum output 837 mg.; in patients with gastric ulcer the means were 113 mg. and 478 mg. respectively. The occurrence of a wide variation on either side of these mean volumes is shown in the frequency distribution charts (Figs. 6 and 7).

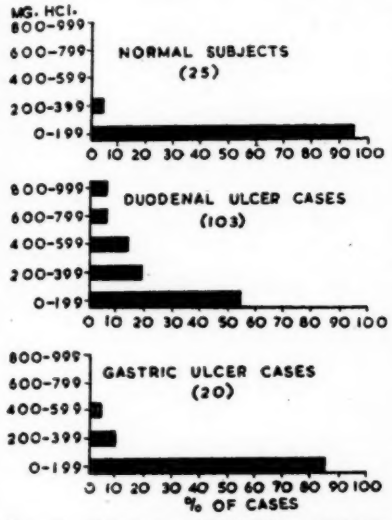

FIG. 6.—Frequency distribution of basal acid output (males).

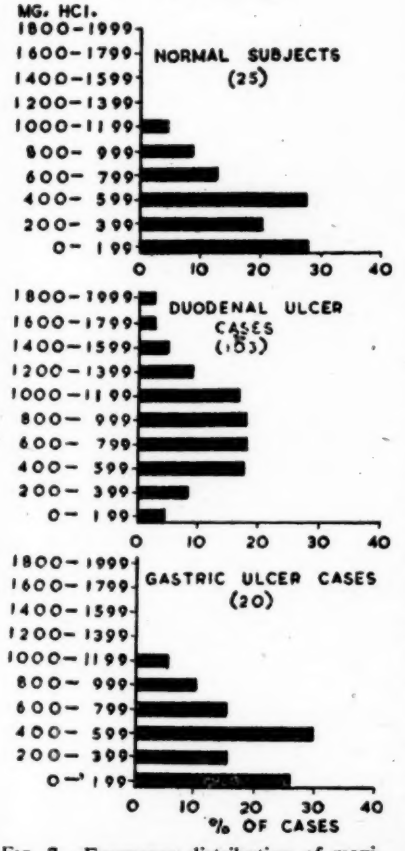

FIG. 7.—Frequency distribution of maximum acid output (males).

Three normal subjects and three gastric ulcer patients were found to have basal anacidity. All showed an acid response after histamine. The presence of stenosis did not appreciably influence either the basal or the maximum acid output in the duodenal ulcer group; a reduction in concentration was compensated by an increase in the volume of juice secreted, so that the actual amount of HCl produced was similar to that in the uncomplicated cases.

Discussion

The gastric secretory response to the commonly employed stimuli of food, alcohol, or small doses of histamine is known to vary greatly from day to day in any one individual. Indeed, the stomach has come to be regarded as capricious in its behaviour. That this is not so has been demonstrated by administering increasing doses of histamine. Four or more B.W. doses of histamine will result in an output of HCl which is constant for an individual and which represents the maximum parietal cell output of acid.

The usual interpretation of an S-shaped curve such as is shown in Figs. 1 and 2 is that the dose-response relationship is of an all-or-none nature. Therefore, with regard to the gastric secretion of HCl, this means that there is no secretion by a parietal cell until an effective stimulus is applied to it; then the parietal cell secretes maximally. The entire population of acid-secreting cells can be stimulated by giving four or more B.W. doses of histamine. Several investigators have attempted to make actual counts of the parietal cells in the gastric mucosa. As accurate counting necessitates detailed examination of the entire stomach, this method can rarely be applicable to human material. Furthermore, the visualization of a parietal cell under the microscope does not necessarily mean that it had been a functioning parietal cell. It would seem reasonable, however, to regard the maximum acid output of a stomach as an index of its parietal cell population.

The routine use of test meals is futile; in selected cases it is of value to determine the presence or absence of HCl. The failure of the stomach to yield gastric juice which was acid to Töpfer's reagent in response to a gruel meal was formerly taken to imply achlorhydria. Until recently, absence of free acid in response to histamine acid phosphate (0.1 mg. per 10 kg.) was regarded as a satisfactory criterion. Palmer and others have shown, however, that, although acid may be absent in several histamine tests, subsequent tests may reveal its presence. In short, the available tests, though satisfactory in most cases, cannot be relied upon to decide the presence or absence of complete achlorhydria. In several of a series of cases believed to have achlorhydria, as indicated by the ordinary histamine test, reinvestigation by the test described here has revealed an appreciable acid response. It should be emphasized that *p*H measurements should be employed in addition to titration methods if small changes in acidity are expected. The application of this test to cases of proved pernicious anaemia has regularly shown a true achlorhydria to be present. The advantages claimed for this augmented histamine test are that it imposes a uniform stimulus which exerts a full load on the acid-secreting cells, and that the results of the test are capable of repetition.

Although the test provides accurate data, its application, like that of all gastric secretory tests, is limited. No narrow standards of normal can be established, and it is consequently difficult to interpret the findings in disease. The observation that duodenal ulcer is associated with a higher range of acid output than normal is in agreement with the accepted work of Bloomfield (1932–3) and Polland (1933). Similarly, the results of the present analysis, which show that the acid output in patients with gastric ulcer varies but little from the output in normal subjects, are not at variance with present beliefs. There is clearly no place for "hypoacidity" and "hyperacidity" as aids to diagnosis. Pernicious anaemia is the only common pathological condition having a characteristic secretory response.

Vanzant *et al.* (1932) found a considerable incidence of "unexplained anacidity" in a study of normal subjects, but not all of these were tested with histamine. Polland (1933) quoted a 9.3% incidence of anacidity to histamine in normals. There were no cases of anacidity to large doses of histamine in the present study. Although the group was a small one, it seems likely that extensive use of the augmented histamine test will reveal a much lower incidence of this "unexplained anacidity."

As no true correlation can be shown between variations in output and pathological states, the main fields of usefulness for the augmented histamine would seem to be in physiological study, in certain anaemias, and in those rare and controversial cases in which peptic ulcer is claimed to exist in the presence of achlorhydria.

Summary

The effects of increasing doses of histamine on the gastric secretion of hydrochloric acid have been studied

in normal subjects and in patients with duodenal ulcer. The dosage required to effect maximum acid output has been established and the duration of this response determined.

An augmented histamine test of gastric secretion, based on these findings, is described.

This test, which imposes a uniform and maximum stimulus on the acid-secreting cells, gives consistent results on repeated estimations in any one individual.

An analysis has been made of the results of the test in 25 normal subjects, 103 duodenal ulcer cases, and 20 patients with gastric ulcer.

I am indebted to Professor C. F. W. Illingworth for his direction and helpful criticism throughout this investigation, to Mr. Gabriel Donald for preparing the charts, and to May and Baker Ltd. for presenting generous supplies of anthisan.

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AN ANTIHISTAMINE IN THE FENESTRATION OPERATION FOR OTOSCLEROSIS

BY

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AND

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As the window in a fenestration operation is made in the vestibular part of the bony labyrinth, signs of a vestibular disturbance are to be expected after the operation. Thus vertigo, with its associated nausea and vomiting, is a constant and sometimes troublesome early sequel, and plays an important part in determining the length of stay in hospital.

In a unit where the demand for beds is always greater than the number available, there is a constant stimulus to search for some means of increasing the rate of turnover of the beds. For some years now we have employed special head and balancing exercises to overcome the vertigo following operations on the labyrinth (Cawthorne, 1946; Cooksey, 1946), but even with these it was not possible to turn a fenestration bed over in less than two weeks.

Because of the immediate post-operative vestibular disturbance it was our practice to keep patients as comfortable and quiet as possible by means of twice-daily injections of soluble phenobarbitone. The disadvantage of this treatment was that the patients were made very drowsy; and vertigo was rarely sufficiently controlled for them to be fit to move to the gymnasium for exercises in under five days. We therefore started to search for a more effective means of controlling the vertigo without causing too much drowsiness, and this brings us to "avomine" (promethazine-8-chlorotheophyllinate). This contains one of the most active of the antihistaminic drugs, promethazine hydrochloride, combined with theophylline and in a form suitable for ambulant patients. It was introduced primarily for the treatment of travel sickness, and its success in this condition suggested that it might help in our problem. Campbell (1949) has already reported on the value of another preparation, dimenhydrinate ("dramamine"), after the fenestration operation.

We first used avomine in our fenestration cases in July, 1951, and to date it has been given to nearly 300 patients. Treatment is started as soon as the patient is admitted to hospital, the day before operation. We have found that a dose of 50 mg. three times daily usually suffices, and this dosage is continued for two weeks after operation.

Results

The results of avomine therapy have been striking, and may be summarized as follows.

Post-operative Vomiting.—Formerly vomiting was often troublesome for two or three days after operation. Since the introduction of avomine vomiting is rare once the patient has recovered from the anaesthetic. With regard to the effect of the anaesthetic on the post-operative course, it has been found that the agents used rarely cause vomiting once the patient is fully conscious. The anaesthetics have been given by Dr. V. F. Hall and Dr. S. A. Mason; after premedication with "omnopon" and scopolamine, in half the cases intravenous thiopentone only was used, whilst in the other half this was supplemented with intravenous pethidine and gas-and-oxygen.

Diet.—Because of the vomiting patients rarely ate solid food for the first two or three days after operation. Now they welcome a light diet the day after operation and usually enjoy normal food the day after that.

Drowsiness.—Continued drowsiness caused by prolonged sedation with barbiturates no longer occurs.

Getting Up.—Formerly patients were reluctant to leave their beds within four days of operation, but now they get up on the second or third day.

Exercises.—The head and balancing exercises can now be started in bed the day after operation, and they go down to the gymnasium to join the class on the fourth day. Formerly they were reluctant to do this before the sixth or seventh day.

Walking.—Whereas patients were unable to walk steadily unaided for about ten days, they can do so now as a rule by the sixth day.

Discharge.—Patients are able to leave hospital on the seventh post-operative day, thus enabling a fenestration bed to be turned over each week.

Micturition.—It is not uncommon for patients to have difficulty with micturition following operations on the labyrinth. This complication has become much less frequent with avomine.

Since the introduction of avomine, and although four or five fenestrations are performed each week, not a single patient has had to be kept in hospital longer than seven days because vertigo was not sufficiently controlled. Perhaps the most convincing proof of its success is given by patients who have had a fenestration operation performed on each ear—one before and the other after we started using avomine. Almost without exception they have commented upon how much less disturbing they found the second compared with the first operation. So far we have not observed any unpleasant side-effects, and it has not been necessary to withdraw the drug in any case.

We would like to thank Messrs. May and Baker for providing the avomine used in some cases of this series.

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A HUMAN BLOOD-GROUP CHIMERA

BY

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Mrs. McK., a donor aged 25, gave her first pint of blood in March of this year. When the blood came to be grouped it seemed to be a mixture of A and O cells, for anti-A serum caused large agglutinates to appear to the naked eye, but the microscope showed these agglutinates to be set in a background of unagglutinated cells. The appearance was such as might be seen for a time after a large transfusion of O blood into an A recipient: but Mrs. McK. had never been transfused. Further samples excluded the possibility of any accidental mixing of bloods.

The evident mixture of blood called to mind the work of Owen (1945) on "immunogenetic consequences of vascular anastomoses between bovine twins." Anastomoses are usually present between bovine twin embryos; primordial red cells belonging to one twin take root in the other twin and continue throughout the life of that animal, to produce red cells with genetically foreign antigens. Chorionic vascular anastomosis and transfer of endocrine secretions between bovine twins of different sex had been postulated as the cause of the freemartin condition by Lillie as early as 1916.

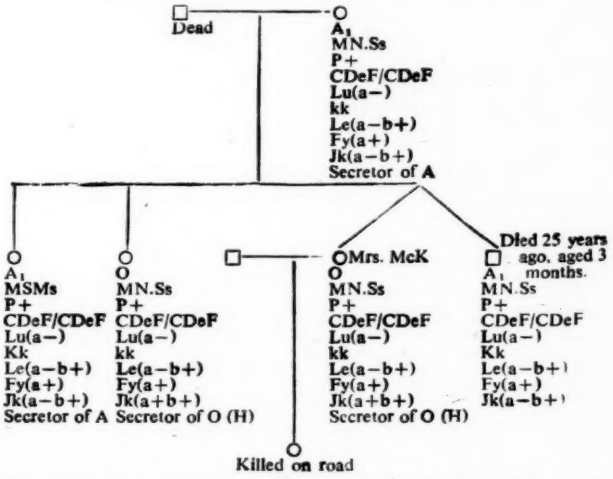
When asked if she were a twin, Mrs. McK., somewhat surprised, answered that her twin brother had died 25 years ago at the age of 3 months. The cause of death was said to be pneumonia complicating a strangulated inguinal hernia.

The O and A_1 cells in the blood of Mrs. McK. can be separated. The result of grouping the two components is shown in the pedigree; the O cells are kk, Jk (a+b+), the A_1 cells are Kk, Jk (a−b+): in their other groups they do not differ. There is no doubt that the true genetic blood groups of Mrs. McK. are those shown under her name in the pedigree. This is established by the fact that she secretes O (H) antigen in her saliva but does not secrete A antigen. Since the red cells of her twin are A_1, Le(a−b+) he must have secreted A. It is strange that we should be able to group completely this twin 25 years after his death.

Miss Marie Cutbush, of the Medical Research Council Blood Transfusion Research Unit, has counted the relative numbers of the two kinds of red cells: 61% are Group O (σ=1.7%), which does not differ significantly from the count made by Miss Cutbush one month earlier.

Mrs. McK. is the first human being to be shown to have a double set of blood groups, and there can be little doubt that one set is the consequence of vascular communication with her twin. Though we have been prepared for this discovery by the work of Owen on bovine twins, such a mixture of blood cannot be common in human twins: the Blood Group Research Unit has tested the blood of 58 pairs of dissimilar twins and 82 pairs of apparently identical twins without finding any evidence of mixed blood groups.

Alternative explanations have been considered: somatic mutation is excluded because three separate genes are involved, and dispermia is highly improbable, for Mrs. McK. shows no obvious sign of asymmetry. None of the blood samples from the other surviving members of the family was in any way unusual.


Dead
A1 MN.Ss P+ CDeF/CDeF Lu(a−) kk Le(a−b+) Fy(a+) Jk(a−b+) Secretor of A
A1 MSMs P+ CDeF/CDeF Lu(a−) Kk Le(a−b+) Fy(a+) Jk(a−b+) Secretor of A
O MN.Ss P+ CDeF/CDeF Lu(a−) kk Le(a−b+) Fy(a+) Jk(a+b+) Secretor of O (H)
Mrs. McK
O MN.Ss P+ CDeF/CDeF Lu(a−) kk Le(a−b+) Fy(a+) Jk(a+b+) Secretor of O (H)
Died 25 years ago, aged 3 months.
A1 MN.Ss P+ CDeF/CDeF Lu(a−) Kk Le(a−b+) Fy(a+) Jk(a−b+)
Killed on road

The blood groups of Mrs. McK. and of her family. The groups shown under Mrs. McK. are those which she inherited and about 61% of her red cells are stamped with these groups. About 39% of her red cells are of the groups shown under her twin brother. The antisera used to group the family and the two components of Mrs. McK.'s blood were: anti-A-A_1,-B-"O"-H, anti-M-N-S-s, anti-P, anti-C-c-Cw-D-E-e-f, anti-Lu^a, anti-K-k, anti-Le^a-Le^b, anti-Fy^a, anti-Jk^a-Jk^b.

Apart from its general interest the case of Mrs. McK. has particular implications:

(*a*) The early presence of A antigen has presumably inhibited the production of anti-A. Mrs. McK. is group O and her serum contains anti-B, but there is no detectable anti-A: it has been looked for by methods using saline, albumin, anti-human globulin, trypsin, and papain. If anti-A were being produced by Mrs. McK. and promptly adsorbed, the only tissue capable of such adsorption would be her A_1 cells, but these cannot be shown to be either sensitized or blocked.

(*b*) Secretion of A antigen in saliva clearly must depend on the presence in the genotype of the A gene as well as the secretor gene, for the secretor gene of Mrs. McK. cannot command the secretion of A present only in her circulation.

(*c*) Mrs. McK. is feminine in appearance and has had one child: she is clearly not a freemartin. Nevertheless, now that it is established that there can be prenatal communication between the circulations of dissimilar human twins, it may be worth recording the proportion of twins among people suffering from infertility and from abnormal sexual development.

In 1916 Lillie wrote: "In the case of the free-martin, nature has performed an experiment of surpassing interest." No doubt the same could be said of Nature's experiment on Mrs. McK. were we able to appreciate more of its implications.

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The World Health Organization Area Representatives' Conference held recently in Delhi approved a proposal that W.H.O. should assist the Ceylon Government to initiate a postgraduate course for nurses in administration and training at the Colombo Nurses Training School: at present, nurses from Ceylon are sent abroad for postgraduate training. The Area Representatives Conference also agreed to the provision of a principal and three nursing tutors for a nurses' training school to be established at Galle or Jaffna in Ceylon. W.H.O. will also give Ceylon help in controlling tuberculosis, venereal diseases, and leprosy.

REACTIVATION OF VARICELLA VIRUS BY CORTISONE THERAPY

BY

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AND

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The following case history is worthy of publication in view of the recent widespread use of cortisone and the fact that similar cases will undoubtedly be observed.

Case History

The patient, a European boy, was first seen at the age of 9 years in June, 1950, when, following a procaine penicillin injection for an infected dog bite, he developed a very severe giant urticaria which caused a serious illness lasting five weeks. He showed little or no response to the usual treatment available at that time—that is, calcium intravenously and orally, antihistaminic drugs, and adrenaline injections. After this illness he was skin-tested against a wide range of possible allergens, including procaine penicillin, and penicillin and procaine separately, with negative results in every case.

On November 6, 1952, he again developed a rash, which his mother feared might be a return of his urticaria. However, on examination he was found to be suffering from a typical though mild attack of varicella, from which he made a complete and rapid recovery.

On November 26 he once more developed giant urticaria; the causal factor may possibly have been penicillin ointment applied to a scratch on his knee a few days before. In view of his previous serious illness it was thought justifiable to give him cortisone, and he was started on cortisone acetate orally, 1 tablet (25 mg.) four times a day. As adjuvant treatment he was given intravenous calcium gluconate, 10 ml. of 10% solution, on three consecutive days. The urticaria responded rapidly, and after seven days his skin was clear. At this stage the cortisone therapy was stopped and within two days there was a slight recurrence of the urticaria. He was put back on to cortisone, the same dosage as before; it once again rapidly controlled the urticaria, but on the third day he developed another rash, which on examination seemed to be a typical chicken-pox rash, but very much more severe than a month previously. The cortisone was stopped immediately; the chicken-pox rash again followed the usual course of cropping for three or four days, with scabbing and full clearance within about ten days. His sister, who was in contact with him, developed chicken-pox fourteen days after his second attack made its appearance.

The likely explanation in this case is that the reactive mechanism of the patient's body was so altered by the cortisone that the varicella virus lying dormant in the tissues after the first attack was allowed to become reactivated, to produce the second clinical attack.

A series of articles on the part nurses can play in the prevention and care of atom-bomb casualties was published recently in the *Nursing Mirror*, and the articles have now been reprinted in the form of a booklet. They have been written specially by lecturers from the Radiological Defence Course at the Royal Naval Medical School, and explain the elementary principles underlying atomic explosions and their effects on the human body, and give advice on medical and nursing treatment. The booklet, which will interest both nursing teaching staff and student nurses, is available from the *Nursing Mirror*, Dorset House, Stamford Street, London, S.E.1, price 1s. 9d. (postage 3d.).

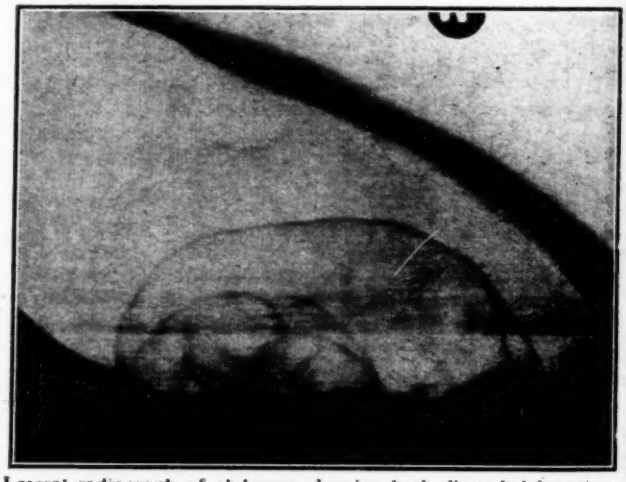
Medical Memoranda

Delayed Traumatic Rupture of the Intestine

A man aged 42 was admitted to hospital in the early hours of January 1, 1952. He had been celebrating the arrival of the New Year and had fallen from a window.

As the result of this fall he sustained numerous fractures, including a fracture of the upper end of his right femur, a fracture of the lower third of the right tibia, crush fractures of the first and second lumbar vertebrae, and fractures of the eighth to the twelfth right ribs. His general condition was poor, but he had no evidence of any intra-abdominal lesion. His abdomen was quite soft and there was no tenderness. The usual resuscitative measures were instituted and the fractures were dealt with by standard orthopaedic methods. There was a gradual improvement in his condition, but for two days he was unable to pass urine and had to be catheterized. He was examined carefully on several occasions by competent observers but no abnormal intra-abdominal signs were detected. On January 5 he first complained of slight abdominal discomfort, but there was no tenderness or rigidity, and bowel sounds could be heard. An *x*-ray film of the abdomen at this time was normal. It was thought that this pain was probably associated with his fractured ribs.

On January 7 his condition deteriorated suddenly and he vomited and complained of abdominal pain. Examination



Lateral radiograph of abdomen showing both distended intestine and gross pneumoperitoneum.

of the abdomen now revealed some tenderness, rigidity, and distension for the first time since the accident, and it was thought that an intra-abdominal lesion was present. Careful watch was maintained for a few hours, and during this time there was a very rapid increase in the distension, the abdomen becoming like a drum. A film of the abdomen taken at this time showed an enormous volume of intraperitoneal gas (see Fig.). It was evident that perforation of a hollow viscus had taken place, and the patient was prepared for laparotomy.

Under a general anaesthetic, given by Dr. E. Frayworth, the abdomen was opened through a long right paramedian incision. There was a free escape of gas as soon as the peritoneal cavity was opened. A little blood and pus was present in the region of the caecum, which was very distended. There was a haematoma of some size behind the caecum and ascending colon. Careful inspection of the caecum revealed a small valve-like perforation through which gas was escaping. There were other areas in the caecum of doubtful viability. No other intra-abdominal lesion was found. It was thought best to carry out right

hemicolectomy, and the continuity of the intestine was restored by means of an isoperistaltic, side-to-side ileo-transverse anastomosis.

The patient made a good recovery from the operation and was eventually discharged to his home when the fractures had united. He later returned to work.

COMMENT

This case is of interest, for it was practically a week before any symptoms or signs of an intra-abdominal lesion appeared. Had it not been for the multiple fractures it is quite possible that this patient would not have been admitted to hospital, or, if he had been, he might have been discharged before the intestinal perforation became manifest.

It is of interest also to speculate on the possible mechanism of the perforation of the caecum. We believe that minor damage to the caecum resulting in a haematoma in its wall occurred after the injury. It is well known that intra-abdominal traumatic lesions are common at the sites of junction of fixed and mobile intestine. The retroperitoneal haematoma probably caused some degree of ileus and caecal distension. The latter eventually became severe enough to cause the bowel wall to give way at the site of a haematoma.

We are indebted to Mr. J. Grant Bonnin, orthopaedic surgeon to the Central Middlesex Hospital, for permission to publish this case.

J. W. P. GUMMER, M.S., F.R.C.S.
G. N. RANKING, F.R.C.S.

Neurological Presentation of Glandular Fever

Neurological complications of glandular fever are not common. The following case is recorded because of its rarity in that cerebellar dysfunction provided the presenting symptoms.

CASE REPORT

The patient, a male shop-assistant aged 18, had been fit and well until about three weeks before admission to hospital, when he had an influenzal illness, with frontal headache, sore throat, and general malaise, which was treated with aspirin. Four days later he developed mild jaundice which lasted a day or two. He was confined to bed for two days, and subsequently felt well. Two weeks before admission he noticed that his legs were becoming weaker, and that there was a gradually increasing loss of balance and incoordination of his arms and legs. His handwriting became irregular, and while standing or walking he had to hold on to something to prevent his falling. In himself he felt well. There was no disturbance of speech, hearing, vision, appetite, bowel action, or micturition, nor any other complaint.

His past history included only chicken-pox and whooping-cough as a child. There was no known contact with any similar cases, with or without jaundice. There was no history of food or other poisoning, or of exposure to leptospires. His family were all fit, apart from his mother, who had a lymphatic obstruction of the right leg. There was no family history of neurological or other disease.

On examination when admitted to hospital on January 14, 1952, he was a slender but well-built youth. He was afebrile. His pulse was 68. No abnormality was detected in the cardiovascular and respiratory systems. The throat was healthy. Abdominal examination did not reveal any abnormality. The pupils gave a sluggish reaction to light, but otherwise were normal; there was no nystagmus; the fundi and cranial nerves were normal. In the upper limbs there was slight weakness of both triceps, and slight weakness and wasting of the small hand muscles: the biceps-jerks were present, the triceps-jerks weak, and the supinator-jerks absent; there was mild ataxia, but no muscle tenderness or sensory disturbance. The lower limbs showed gross bilateral pes cavus, slight weakness of extensors of hips, moderate ataxia, absence of both knee- and ankle-jerks, plantar responses both flexor, and no muscle tenderness or sensory disturbance. There were no meningeal signs or trunk weakness. Abdominal reflexes were present and equal. There was a very ataxic gait, and Romberg's sign was present. Multiple, discrete, non-tender glands were palpable in both anterior and posterior triangles of the neck, from clavicles to mastoids, and also small glands in the axillae. The spleen was not felt. The epitrochlear glands were also palpable.

A provisional diagnosis was made of mild peripheral polyneuritis, with additional cerebellar signs, the result of a recent infection, probably glandular fever.

Investigations.—Cerebrospinal fluid: clear; pressure 170 mm.; no block; protein, 80 mg./100 ml.; chlorides, 690 mg./100 ml.,; the film showed a very occasional lymphocyte, no organisms; culture was sterile; Wassermann reaction, negative; Lange colloidal gold curve, normal. Blood: haemoglobin, 108%; red cells, 5,620,000; white cells, 6,600 (polymorphs 52%, small lymphs 19%, large lymphs 25%, monocytes 3%, and eosinophils 1%); sedimentation rate: 8 mm. in 1 hour (Wintrobe); Wassermann reaction, negative. Paul–Bunnell test (January 16): sheep cells agglutinated to a titre of 1 in 16,384; guinea-pig kidney absorption titre, 1 in 8,192. Liver-function tests (January 24): alkaline phosphatase, 19 K.A. units/100 ml.; van den Bergh direct reaction, negative; 1.4 mg. bilirubin/100 ml.; thymol turbidity, 2 units/100 ml.; cephalin cholesterol, +++. An *x*-ray film of the chest did not show any abnormality.

Progress was satisfactory. The patient was well in himself the whole time, and throughout was afebrile. He was discharged home one month after admission, no specific treatment being necessary. When last seen as an out-patient 14 weeks after the onset of the symptoms he was in good health; the ankle-jerks, however, were still absent. There were almost no palpable glands, and the Paul–Bunnell and liver-function tests, which had been performed frequently, were now within normal limits.

COMMENT

Glandular fever is not an uncommon disease, and the presence of possible neurological complications is becoming increasingly recognized. It is seldom that the neurological complications provide the main features of the illness, and it is probably extremely rare for cerebellar dysfunction to provide the presenting symptoms.

Crowther (1951), reporting a case of glandular fever with encephalitis, reviewed the literature and could find only 24 cases of glandular fever confirmed by the Paul–Bunnell reaction and involving the nervous system since 1931, although several clinically suggestive cases without a positive Paul–Bunnell reaction have been described. Similarly, abnormal cerebrospinal fluids have been found without clinical manifestations. Of the 24 cases he quoted, 4 had a pure encephalitis, the others showing encephalomyelitis, cranial nerve lesions, meningitis, and peripheral nerve lesions. Another case with cerebral complications has since been reported by Librach (1952), who discussed possible ways in which the nervous system may become involved, and suggested that there may be an allergic origin.

The present case is unusual in several respects: the neurological symptoms were the presenting features, not merely complications; at no time after admission to hospital was the patient febrile; the cerebrospinal fluid showed only an increase in the protein content. The suggestion is therefore made that in cases of atypical infections of the nervous system the diagnosis of glandular fever should be considered.

I am indebted to Dr. I. Gordon, under whose care the patient was admitted, for his constant encouragement.

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Reviews

TREATMENT OF POISONING

The Symptoms and Treatment of Acute Poisoning. By Professor G. H. W. Lucas. (Pp. 320. £1 7s. 6d.) London: H. K. Lewis and Co. 1953.

The danger of accidental, suicidal, or homicidal poisoning by the older galenical drugs or by certain species of plants, which has been a perpetual source of interest for hundreds of years, has nowadays been increased by the introduction of numerous potent new remedies into therapeutics, by the widespread use of agents to destroy pests of all kinds, and by the use of toxic substances in industry. It is fortunate that the treatment of poisoning is now more effective than it used to be. This little book provides concise and up-to-date information on the symptoms and treatment of acute poisoning by most of the agents likely to be encountered in medical practice. It is entirely concerned with the results of overdosage and not with the side-effects of drugs given in therapeutic quantities or with reactions arising as the result of idiosyncrasy in the patient.

Children are particularly liable to accidental poisoning owing to their singular propensity to investigate with their mouths substances which excite their curiosity. This danger is increased by the modern tendency of pharmaceutical firms to market their tablets and capsules in attractive and vivid colours and to temper their elixirs with the most fascinating flavours. In consequence a chapter of the book is devoted to the management of poisoning in children. A table is provided giving domestic equivalents for solid and liquid antidotes which may have to be measured out quickly in an emergency, and another showing for many poisons the least fatal dose recorded in the literature and the largest dose from which patients have recovered—information which may prove valuable to a doctor under cross-examination in a court of law. A complete index with adequate cross-references enables the reader to locate quickly the desired information. The book tells the doctor in short, sharp sentences, mostly in the imperative mood, what to do in an emergency and does not cloud the issue by stopping to reason why. The advice is usually scientifically sound, and it is a comfort to read in a work on poisoning that the skilful use of the stomach tube has largely superseded emetics. The book can be confidently recommended to general practitioners.

D. M. DUNLOP.

CHILDREN'S DISEASES

Fanconi and Wallgren's Textbook of Paediatrics. Edited by W. R. F. Collis, M.D., F.R.C.P., F.R.C.P.I., D.P.H. Translator and Co-editor E. Kawerau, M.B., M.Sc., A.R.I.C. (Pp. 1,104; 440 figures. £7 7s. 2d.) London: William Heinemann. 1952.

This book first appeared as Fanconi and Wallgren's *Lehrbuch der Pädiatrie*, and Dr. W. R. F. Collis, with the assistance of Dr. Kawerau as translator and co-editor, has been responsible for the new edition in English. The opportunity has been taken of making revisions in the original text, and a new section on megacolon by Dr. M. Bodian has been added. The numerous authors are all highly distinguished paediatricians, and their book is a considerable volume of some 1,100 pages, with over 400 illustrations, most of which are of high standard; the coloured plates are wonderfully good.

The book is planned on the usual textbook lines, system by system. Separate chapters are devoted to certain diseases and to particular aspects of paediatrics—for instance, tuberculosis, juvenile rheumatism, syphilis, and nutrition. The authors have been allowed a good deal of latitude, and they have responded by giving their personal views; this always makes for interesting and stimulating reading. The book is likely to be more suited to the hospital paediatrician than to the general practitioner, who is helped by stronger emphasis on the early symptoms and signs of disease and by fuller reference to the scope of prophylaxis. The chapter on the disorders of puberty and adolescence—a subject that often receives scanty notice in textbooks—is an exception to the above comment, and is to be warmly welcomed.

The reader who is accustomed to the English textbooks will find some charts and tables that present facts in a new and stimulating fashion. But he will also find many mistakes in spelling and punctuation, and some paragraphs that appear to have defeated the skill of an earnest and competent translator. Doubtless these errors will be corrected in the next edition, and the work should prove to be a valuable addition to paediatric libraries.

N. B. CAPON.

ACUTE RENAL FAILURE

Acute Renal Failure: Including the Use of the Artificial Kidney. By John T. MacLean, M.D., F.R.C.S.(C.), F.A.C.S. (Pp. 114; illustrated. £2 7s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953.

There is much useful information in this little book, though none of it is new. Modern views on the causes, pathology, and treatment of acute renal failure are adequately presented and evaluated, though so outstanding an example of the condition as cortical necrosis of the kidneys would seem to have been overlooked. Prognosis also could have been discussed more fully. The description of the uses, application, and limitations of the various forms of the artificial kidney and other methods of dialysis is excellent, and the author's warning of the inadequacy of rigidly standardized solutions for perfusion therapy is important and timely.

The book is well written, contains many informative case records, tables, graphs, and illustrations, including five coloured plates, and concludes with an adequate subject index. The production is admirable, and the book can be recommended as a useful introduction to the subject.

A. A. OSMAN.

PSYCHOSOMATIC MEDICINE

Psychosomatic Medicine: Its Principles and Applications. By Professor Franz Alexander, M.D. (Pp. 300. £1 1s.) London: George Allen and Unwin. 1952.

The author of this book is the director of the Chicago Institute for Psycho-analysis, the first such institute with funds adequate for the necessarily prolonged research combining psycho-analytic and physiological observations on patients presenting combined psychiatric and medical problems. He has written and collaborated in writing many other more specialized books, but this volume should make a general appeal to senior medical students and general practitioners as well as young psychiatrists and specialists in the fields covered. The basic postulate of the author's approach is "that the psychological factors influencing physiological processes must be subjected to the same detailed and careful scrutiny as is customary in the study of physiological processes. Reference to emotions in such general terms as anxiety, tension, emotional imbalance is outdated. . . . Only such studies are included in this book as are carried out in accordance with this principle." The bibliography of 260 references is mostly to recent publications.

The first third of the book is a concise, clear exposition of the present American marriage of the detailed psychopathological principles of the pupils of Freud and the multidimensional approach of the pupils of Adolf Meyer. The remainder of the work is on gastro-intestinal disturbances (anorexia, bulimia, vomiting, cardiospasm, peptic ulcer, chronic diarrhoea, spastic and mucous colitis, ulcerative colitis), respiratory, cardiovascular, skin, metabolic and endocrinal, and joint and skeletal muscular disturbances. In a final chapter Benedek discusses male and female disorders in accordance with the principles outlined above. Many excellent half-page histories of psycho-analytic treatment or of psychiatric treatment by psycho-analytically

trained psychiatrists are included. The reasons for and the difficulties of co-operation between psychiatrists and physicians are clearly stated.

This book reads easily and is brief when compared with the material psychiatrists usually write. The psychiatric concepts should be understood by all physicians as easily as the medical student will understand the physiological concepts. What is hidden perhaps is that, whereas both psychiatrists and physicians take for granted the judgment and experience necessary to make use of the physiological principles, physicians have more difficulty in recognizing the need for psycho-analytic training taken by the psychiatrists whose basic studies have made this book possible. One can only hope it will be read as much in preparation for medical examinations as it surely will be for psychiatric. The nearest comparable book is Stanley Cobb's popular *Foundations of Neuropsychiatry*, first published in 1936.

W. CLIFFORD M. SCOTT.

CARDIOGRAPHY IN GENERAL PRACTICE

Cardiography in General Practice: Electrocardiography, Vectorcardiography, and Ballistocardiography. By Abraham I. Schaffer, M.D. (Pp. 136; 55 illustrations. £1 4s.) London: Baillière, Tindall and Cox. 1952.

The author of this book seems to aim at giving general practitioners a modern account of electrocardiograms based on a simple exposition of the physiological facts, and he succeeds very well indeed. It is remarkable how much information is compressed into a small space. The expression throughout is clear and concise, and there is no taking refuge in pseudo-scientific jargon. The result is that as a rule it is easy to follow the reasoning. At times perhaps the author is didactic; at times the exposition is too brief for anyone starting to learn the subject. On page 66 it is not made clear how to distinguish the minor variations seen in the cardiogram on exercise and acceleration from those of pathological significance. The Q wave which appears over an infarct is said to be due to a vector pointing from the contact. The idea of a "window" in the wall of the ventricle is not mentioned. It is not easy to see how the vector can distinguish between infarcts on the posterior wall of the ventricle from those of the diaphragmatic surface (p. 109). But the chapter on vectorcardiography is made clear and simple and well worth reading. There is no doubt that the idea of interpretation by vectors would clear up many difficulties the beginner meets, if he is not frightened of this formidable subject. This account need not deter the beginner, who will soon find that "new presbyter is but old priest writ large." The diagrams are simple. There is also a chapter on ballistocardiography. This is a good little book and one deserving, and needing, very careful study.

TERENCE EAST.

EARLY DIAGNOSIS OF CANCER

Fundamentals of Clinical Cancer: With Emphasis on Early Diagnosis and Treatment. By Leonard B. Goldman, M.D. (Pp. 312 221 figures. $8.75.) New York: Grune and Stratton. 1953.

This book is intended for all who diagnose and treat cancer. Its aim is to make practitioners cancer-conscious so that they suspect the disease in its early stages, and to show how the diagnosis may be confirmed and what treatment should be given.

Some of the author's views differ from those usually held in Britain. Facing page 1 are 10 commandments of cancer control. Many readers here will disagree with the first—"Circumcise at birth to prevent cancer of the penis, and to reduce the incidence of cancer of the cervix and cancer of the prostate"—and the last—"Do not operate on tumours which cause continuous pain except bone tumours." Some operable cancers cause continuous pain, and most non-malignant painful tumours require drainage or removal. The author lays great stress on biopsy; the methods of localized removal by scissors and by punch illustrated in Figs. 1 and 2 would be anathema to most British surgeons and pathologists. Other statements to which exception may be taken are that "early cancers may be removed by simple surgery, invasive cancers should be eradicated by radical surgery," that "squamous cell cancers on the skin of the face rarely metastasize," and "every enlargement of the testicle should be biopsied by removal of the testicle." The view that "70% of lung cancers can be seen through the bronchoscope" is unduly optimistic, but the assertion that "occasionally cancer of the lung can be removed by radical surgery" is quite unjustifiably gloomy. About 20% of lung cancers can be resected, and a quarter of the patients thus treated are alive five years later.

Apart from these minor criticisms, the book is excellent. It will not interest the specialist surgeon or the radiologist, for treatment is not discussed in any great detail, but it should be of considerable help to general practitioners. The common types of cancer in each region are described. Methods of diagnosis and differential diagnosis are given, as well as the different methods of treatment available, with advice on which is most suitable. The illustrations, which are numerous, well chosen, and well reproduced, are an admirable feature.

HENEAGE OGILVIE.

GYNAECOLOGICAL PATHOLOGY

Gynecological and Obstetrical Pathology. By Professor Peter A. Herbut, M.D. (Pp. 683; 428 illustrations on 246 figures and two coloured plates. £4 13s. 6d.) London: Henry Kimpton. 1953.

The size and title of this book raise hopes that it is the one for which all gynaecologists and pathologists have been waiting. Unfortunately its title is rather deceptive in that its size is explained not by an abundance of pathology but by an attempt to cover every condition from every approach—its incidence, cause, clinical features, complications, diagnosis, and even treatment and prognosis. The only real justification for including obstetrics in its title is a chapter on diseases of the placenta and membranes, a chapter notable for the statement that "infarcts of the placenta, even when massive, are of little clinical significance."

The discussion of clinical aspects by a laboratory worker must almost inevitably be based on reading and hearsay rather than on experience, and here the reader gets the same impression of the sections on morbid anatomy and histology. Instead of giving his own views and observations Dr. Herbut is content to treat most subjects by giving a précis of some article which has appeared in the medical press at some time during the last ten years. The review of the literature, confined almost entirely to journals published in the U.S.A., is incomplete and could be positively misleading. For example, the author states that he can find only two recorded cases of air embolism resulting from vaginal insufflation, whereas references to four such cases were given in the *British Medical Journal* as long ago as 1945, and there has been at least one other published since. Again, can we really believe that only 28 cases of female pseudohermaphroditism had been described by 1942?

In a wide coverage of the field some account is given of many rare and bizarre conditions whose description is not easy to find elsewhere, and this is the most useful feature of the book. Unfortunately, one's confidence in it as a work of reference to the rarities is shaken by the many errors and discrepancies which are to be found in regard to the conditions on which one has some prior knowledge. The statement that the cause of uterine fibroids is now known is as startling as it is untrue. Erosion of the cervix—a fascinating problem for pathologists—is mentioned only once, to be dismissed as synonymous with ectropion. Fig. 114 is upside down. Fig. 175 is alleged to show a serous cystadenoma of the ovary, whereas the arrangement of the blood vessels in its wall shows clearly that it is an extraperitoneal cyst—probably fimbrial or parovarian in type. Ovarian agenesis is said to represent a failure in the development of the part of Mullerian duct which gives rise to the ovary. The book is a queer mixture and, on the whole, disappointing.

T. N. A. JEFFCOATE.

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THE ARTIFICIAL HEART

Research into the creation of an artificial circulation has been going on since 1937, when Gibbon[1] reported the use of a heart–lung apparatus to maintain the circulation during experimental occlusion of the pulmonary artery. Dr. D. G. Melrose and his colleagues have now brought such an apparatus to a high degree of perfection, and their results are published in our opening pages this week. The design of their machine is based on that of the pump-oxygenator described by Björk[2] and Crafoord.[3] The oxygenator is a rotating cylinder set at an angle to the horizontal and containing annular perspex plates. The blood travels through it under the influence of gravity and is spread over the plates. These are arranged so that the greatest possible surface area of blood is exposed to the oxygen pumped into the cylinder. Two valveless rotary type pumps, driven by electric motors, are used: these are a venous pump to supply the oxygenator with blood, and an arterial pump to deliver the oxygenated blood to the subject. Three manometers measure, respectively, the volume of blood in the oxygenator, the pressure in the venous part of the artificial circuit, and the pressure in the arterial part of the artificial circuit. The speed of the pumps is controlled electrically by signals from the manometers, thus ensuring that they work in harmony to maintain blood volume and arterial pressure; excessive venous suction is thus prevented. This mechanism is capable of maintaining the blood volume within 50 ml. over a range of flow of between 300 ml. and 3 litres per minute. The oxygenator is kept at a constant temperature, and oxygen is delivered through an adjustable rotameter which permits of adjustments of rate of flow. The acid–base balance is controlled by altering the rate of flow of oxygen or by the addition of small amounts of carbon dioxide. The gases are passed through a warming, filtering, and humidifying system.

In the second paper published in this issue Melrose and his colleagues describe the results in thirty anaesthetized dogs of using the heart–lung machine in parallel with the normal circulation, blood being fed into the machine from the femoral vein and returned to the animal via an artery. Careful studies have been made of cardiac output, central venous pressure, systemic blood pressure, and cardiac rate and rhythm, as well as investigations into the effect of the oxygenator on the cellular and chemical constituents of the blood. In order to prevent coagulation in the oxygenator the animals were heparinized initially, and then given protamine sulphate to neutralize the heparin at the end of the experiment. Most of the experiments lasted one hour, the rate of perfusion being 750–1,000 ml. per minute. No dog died as a direct result of the perfusion, although for other reasons four did not survive the procedure. Two to three days later the surviving dogs were normally active and apparently had suffered no ill effects. Post-mortem examination of 25 dogs, which were sacrificed three months later, did not show any abnormalities.

The results obtained are of great interest, and there can be no doubt of the efficiency of the machine as an oxygenator: for instance, in one dog 150 c.cm. of oxygen was introduced into the circulation per minute. When dogs were made anoxic by reducing the content of oxygen in the inspired air the arterial oxygen rose significantly in the region where the oxygenated blood was returned from the machine, but remained depressed in other areas. Thus, when the blood was returned to the femoral artery, the cephalic end of the animal remained anoxic, while the oxygen content of the arterial blood in the caudal end increased. Cardiac output determinations on twelve dogs showed that the output fell in nine and rose only in two. In some dogs the fall was of the order of 30%, although the authors point out that considerable difficulty attended the accurate estimation of the output under the conditions of the experiment. No arrhythmias occurred, and there were no significant alterations in heart rate, mean arterial pressure, or central venous pressure. The formed elements of the blood changed in several ways, the most striking being a fall in leucocytes of nearly 50%, mainly the granular series. The numbers of platelets and red blood cells fell also, but to a less extent. The plasma haemoglobin rose, and the haematocrit fell, indicating haemolysis and haemodilution, which were considered to be due in part to the dextran solution used to charge the oxygenator. Cleaning and sterilization of the apparatus was carried out chemic-

1 *Arch. Surg. (Chicago)*, 1937, **34**, 1105.
2 *Acta chir. scand.*, 1948, **96**, Suppl. 137
3 *Surg. Gynec. Obstet.*, 1949, **89**, 629.
4 Helmsworth, J. A., *et al*, *J. thorac. Surg.*, 1952, **24**, 117
5 *J. Amer. med. Ass.*, 1952, **150**, 451.
6 Davies, C. E., and Mackinnon, J., *Lancet*, 1949, **2**, 883.
7 *J. thorac. Surg.*, 1952, **24**, 134.
8 *J. Amer. med. Ass.*, 1952, **150**, 642.
9 Melrose, D. G., and Wilson, A. O., *Lancet*, 1953, **1**, 1266.

ally by detergents and 3% formalin, but sterilization by autoclaving should soon be possible.

Melrose and his colleagues consider, and with justification, that their apparatus might now be applied to the treatment of certain forms of cardio-respiratory failure in man, the oxygenator being used in parallel with the normal circulation. Clearly the step from experiment on the animal to treatment of the human is a big one, and careful thought will have to be given to the type of patient likely to benefit from the artificial heart, and to the problems which may arise. The indications for its use would include any form of acute, potentially reversible anoxia which does not respond to the usual forms of treatment—for instance, acute cor pulmonale, severe congestive cardiac failure, or acute circulatory failure such as may follow cardiac infarction. The oxygenator would also be of great value to the cardiac surgeon to augment the function of the heart during long and difficult operations for the relief of cyanotic congenital heart disease, but heparinization of the patient, which is apparently essential for the working of the oxygenator, would present a formidable problem to the surgeon. Although the coagulation time can be rapidly restored to normal after operation by the injection of protamine sulphate, this may apparently result in acute arterial hypotension.[4] Disadvantages of the oxygenator at present are the difficulties of complete sterilization (with the possibility of introducing pyrogenic or other toxic material into the recipient), the profound fall in circulating white blood cells, haemolysis, and a possible fall in cardiac output. The most important of these are likely to be the reduction in white blood cells and in cardiac output, though the former may prove to be less of a disadvantage than is at first apparent, since the number of white blood cells apparently rapidly returns to normal at the conclusion of the treatment, and may later exceed the original level. Moreover, there was no leucopenia after the use of a pump-oxygenator in man by Helmsworth and his colleagues.[5] Cardiac output is unlikely to fall by more than the output of the machine, but any further reduction in output might be undesirable in an acutely anoxic patient, even though the arterial oxygen saturation was increased.

In heart failure due to chronic bronchitis and emphysema, the respiratory centre may respond only to a low arterial oxygen saturation. In some cases coma and neurological abnormalities have been induced by oxygen administration.[6] If the oxygenator is applied to such patients, measures will have to be taken to ensure adequate pulmonary ventilation and carbon dioxide elimination, and some form of assisted respiration should be at hand. The vein-to-vein, rather than the vein-to-artery, route would appear to be preferable for perfusion, in view of the difficulties and potential hazards of intra-arterial transfusion.[9] Helmsworth and his colleagues[5] used a similar machine to treat a patient with cor pulmonale, drawing blood from the inferior vena cava via a catheter in one saphenous vein and returning it to the other, the arterial oxygen saturation being raised from 43% to 58–65%. No ill effects resulted from the use of the machine, but improvement was not maintained after withdrawal of the artificial circulation.

Professor Ian Aird, in his foreword to Melrose's first paper, wisely suggests that the use of an oxygenator to replace the heart during cardiac surgery may not yet be immediately attainable. Certainly the most formidable difficulties have been encountered by other workers when the whole heart has been excluded from the circulation, such as air embolism or haemorrhage when the venous end of the pump is attached to the right auricle, and acute arterial hypotension and bradycardia when the right auricle is emptied.[7] But Dodrill and colleagues[7] have reported the absence of such hypotensive reflexes from the left auricle, and have succeeded in isolating the left side of the heart in animals by removing blood from a pulmonary vein and returning it to the aorta through a cannula in the subclavian artery. By this means they were able to expose the mitral valve for 20–30 minutes, with subsequent survival. They were also able successfully to by-pass the left ventricle in a patient with mitral-valve disease for 50 minutes, maintaining the artificial circulation at a rate of 4½ litres per minute.[8] If this technique (which, incidentally, does not require the oxygenator) should prove generally applicable, the surgery of mitral incompetence and aortic valve disease would be greatly assisted.

Whatever the future applications of the artificial heart, Melrose and his colleagues are to be highly commended for their ingenuity and resource. The vital step of applying the machine in treatment has presumably still to be taken. The circumstances justifying a trial at the present time are few, but the potentialities of the machine may be considerable. A glimpse of the uses to which a similar machine has been put in the treatment of a desperately ill patient has already been given by Helmsworth *et al.*[7] We can feel assured that this machine will be used wisely and humanely, and it is likely to be a valuable contribution to the advancement of cardiac surgery.

FLUORIDATION OF WATER

For many years it has been observed that the presence of fluorine in drinking water affects the structure of the teeth to a greater or less extent according to the quantity present. McKay reported[1] in the United States in 1929 that the incidence of dental caries was reduced in a district where there was a high concentration of fluorine in the water supply. In consequence a number of field surveys were carried out, and by 1942 it was established that dental caries is less in the groups of individuals who drink water containing fluorine during the period of tooth formation. This has since been confirmed by reports from many other countries, including Great Britain.

United States research workers decided to ascertain whether a similar beneficial effect followed the addition of enough fluorine-containing compound to a fluorine-deficient water supply. The concentration of 1 p.p.m. of fluorine was selected as giving considerable protection against dental caries without mottling of enamel. The first of six projects was started in 1945 at Grand Rapids, Michigan. But more recently fluoridation of drinking waters has been adopted in many communities in the United States purely as a public health measure.

In Britain the Medical Research Council, in a report to the Minister of Health, recommended that a small mission should study the fluoridation of water supplies, and one was therefore sent to the U.S.A. to study the schemes there at first hand. Its 100-page report has just been published.[2]

The mission considers the evidence is conclusive that a reduction in the incidence of dental caries is obtained comparable to that experienced when fluorine occurs naturally in the water. However, since the schemes have been in operation for only seven years, data relating to individuals over the age of 6 years are not yet available. But there is nothing to suggest that water containing naturally occurring fluorine has properties different from those of water to which fluorine has been added.

The possible hazards of adding fluorine have been carefully considered. The risk of producing mottled enamel at the level of 1 p.p.m. is extremely small. Only an occasional white fleck on the enamel occurs, which is so slight that it can be recognized only with experience. No sound evidence was found that there is danger to health from the continuous consumption of water containing fluorine in low concentration. Mortality statistics did not indicate any hazard, and according to local medical opinion there was no increase in morbidity. The mission concludes that "the proving of a negative is extremely difficult. Meanwhile we are impressed by the fact that millions of people are living in ordinary good health on waters containing fluorine at levels of 1 p.p.m. or more."

It may give rise to some surprise that in the United States, "where by 1951 fluoridation of water supplies had become a fairly common practice," a Select Committee of the House of Representatives conducted a public inquiry into the safety and efficacy of fluoridation and concluded "that a sufficient number of unanswered questions concerning the safety of this program exists to warrant a conservative attitude." This conservative attitude is mirrored in the mission's recommendations. It advises in the first instance the addition of fluorides to water supplies of some selected communities which should be regarded as study centres to observe the effectiveness of the procedure under our own particular conditions of diet and caries experience. Research should also be carried out in areas where fluorine occurs naturally and in higher concentrations than that suggested for artificial addition, where the general health could be studied and investigations carried out into bone development and disease, and diseases of the kidney in particular, so that no question remains unanswered.

The amount of reduction in dental caries caused by the presence of fluorine in the drinking water should be viewed in perspective. Comparative studies show that much the greatest change in the incidence of dental caries is associated with alteration of diet. Even the reduction in dental caries experienced by many communities under wartime conditions was greater than could be expected from drinking fluorine-containing water. And the increase in dental caries observed since the war, an increase that seems to be continuing even now, would scarcely be reversed by the fluoridation of drinking water. Even so, such preventive measures as topical applications to the teeth are far less effective. Of the measures available, fluoridation of drinking water to a level that shows a decrease in caries without discoloration of the teeth would seem to be a most useful procedure. Although not every child would necessarily benefit from it, since the water intake might be below average, the greatest benefit to the greatest number of children would result, and its effect would last well into adult life. But in spite of this preventive measure dental caries will be a common disease and nearly everyone will need to have carious teeth treated annually.

Such a measure as fluoridation of public water supplies, entailing the treatment of a commodity consumed by almost everyone, is likely to be the centre of warm controversy. Appealing to primitive

[1] *Dent. Cosmos*, 1929, **71**, 649.
[2] *The Fluoridation of Domestic Water Supplies in North America as a Means of Controlling Dental Caries*. 1953. H.M.S.O. 5s

emotions in which they have a vested interest, some politicians and publicists may try to divert public attention from the facts so far gathered. This report makes an informative and dispassionate contribution to the debate.

A HUMAN CHIMERA

The *chimaera* of classical tradition was a creature consisting of parts of several different vertebrate species. In the natural world individuals composed of two genetically distinct parts are rare. They are found in the plant kingdom and more rarely among insects. In their more obvious manifestations chimeras are unknown among mammals, but serology, more subtle than the unaided eye, has shown that they do exist in cattle. And now Mr. I. Dunsford and his colleagues, as they report in this week's *Journal* at p. 81, have demonstrated the existence of a composite human being.

It has long been known that when cattle twins are of unlike sex the female is usually sterile, and Lillie[1] showed that this was associated with an anastomosis between the chorionic circulations. In the freemartin or imperfect female twin the abnormal genitalia are cytologically female and are the consequence of a transfer of hormones, not of cellular material, from the blood stream of one individual to the other. Owen[2] was the first to show that a cellular transfer can indeed take place. He demonstrated that in non-identical cattle twins, whatever their sex, there is a double set of red blood cells, one set corresponding in its blood-group antigens to the genetical constitution of the individual carrying them, and the other set to the constitution of the twin. To account for this it must be assumed that viable erythroblasts traverse the chorionic anastomosis in each direction, and become implanted in the bone marrow of the opposite twin. Vascular anastomoses between dizygotic twins and abnormalities in the genitalia of twins of unlike sex do not appear to have been described in man, nor have mixed blood groups hitherto been observed in human twins.

The chimera described this week by Dunsford and his colleagues is a woman with a mixture of A and O red cells. She is the survivor of a twin pair. The two sets of cells are distinct genetically, differing in two other antigens as well as those of the ABO system. The authors consider a number of possible explanations and show that almost certainly the case is the result of an antenatal implantation of erythroblasts from the twin, as already described in cattle.

The research described opens up an interesting but limited field of investigation into the blood groups of twins, the anatomy of their foetal blood supply, and, though not present in this case, the possible occurrence in them of abnormalities of the genitalia. But there are some wider implications. The observations reveal a further example of the failure of the organism to become immunized to an antigen to which it has been exposed in early foetal life. Another suspected example of this was recently discussed by Booth *et al.*[3] But perhaps the most fundamental finding was that the genetical control of salivary secretion of the blood group substance does not operate through the red cell at any stage of the cell's existence. This may have a bearing on the recent discovery of a relation between blood groups and the incidence of carcinoma of the stomach[4] and the suggested relation of this to secretion.[5]

1 *Science*, 1916, **43**, 611.
2 Ibid., 1945, **102**, 400.
3 *British Medical Journal*, 1953, **2**, 41.
4 Aird, I., and Bentall, H., ibid., 1953, **1**, 799.
5 Sheppard, P. M., ibid., 1953, **1**, 1220.

UNIVERSITY GRANTS

Great changes have taken place in medical education since the war, according to the latest report of the University Grants Committee.[1] They were in response to the scientific revolution that is still in full spate in our profession and to the proposals of the Goodenough Committee made in 1944.[2] Since then fifty-five new full-time professorial chairs have been created, together with their staffs of readers and lecturers from whom future professors will be recruited. Postgraduate education has been greatly strengthened, notably in the British Postgraduate Medical Federation established by London University. And most of the teaching hospitals have greatly expanded their research programmes. Much the same story can be told of the other branches of science—though with one striking difference. Whereas the total student population rose from 50,000 to 83,000 between 1938–9 and 1951–2, the medical student population showed little change, being 12,000 in the earlier year and 14,000 in the later. So, with fifty-five new professorial chairs to contend with as well as an intern year, the students are likely to share the regret expressed in this report that "little appears to have been done to carry out the recommendations of the Goodenough Committee for a lightening of the medical curriculum." If teachers can ever bring themselves to lighten instead of to increase the load they think their charges ought to bear, some of them will have an opportunity of suggesting how it should best be done when they speak at the First World Conference on Medical Education to be held at B.M.A. House next month.[3]

If the methods and subjects taught have changed in the years reviewed, so too have the students. Though figures for financial assistance are not given separately for medical students, they probably do not differ much from those for all students, of whom 41% received assistance in 1938–9, 72% in 1951–2. But the quality of the students seems not to have altered much. The very clever have remained few, the really weak have not found places; consequently the proportion of good second-class students is higher than it used to be. Apart from that the report finds some evidence of a general improvement of student quality in medicine, attributing it to the fact that entrants come from a wider field than formerly. Inquiring into health services organized by the universities, the University Grants Committee found a strong demand for them from the students, who attached

1 *University Development*. H.M.S.O. 3s. 6d.
2 *British Medical Journal*, 1944, **2**, 121.
3 For programme see *British Medical Journal*, July 4, p. 32.

much importance in particular to psychiatric advice being readily available. But, as the report points out, the coming of the N.H.S. must make universities think again about the expenditure of money on services of this kind lest they merely duplicate what is already provided.

The functions and powers of this committee, which make it unique in university administration, are discharged with such sagacity that not only is it the envy of universities in other countries but—a harder test—it continues to hold the respect of universities in Britain. Its members give abundant evidence of that love of learning whose advancement it is their task to help.

PLASMA EXPANDERS

The introduction of gum acacia solutions by Bayliss and other investigators for infusion into the wounded toward the end of the first world war saved many lives. During the second world war the Allies relied on blood and plasma infusions with notable success, but new plasma expanders were developed, mainly in Sweden and Germany, to help overcome difficulties in supplying sufficient quantities of blood and blood products. These difficulties are still present in many parts of the world, and in certain circumstances even Britain is apt to experience them in spite of the finest of transfusion services. The risks from plasma and blood transfusion have not all been overcome, notably that of plasma jaundice; others are probably still to be discovered. Progress in finding out the advantages and disadvantages of plasma expanders is therefore important.

Two modern plasma expanders are now available commercially—dextran and polyvinyl pyrrolidone. Their therapeutic value in retaining fluid within the circulatory system depends on their colloid osmotic pressure, which is a function of the number of their molecules not free to pass through the blood capillaries. These colloids are unfortunately not homogeneous in molecular size: they usually range from about 20,000 to 200,000 in molecular weight terms. These small and large molecules differ in their effects in the body, not only in degree but also in kind. Substances with molecular weights below about 25,000 are rapidly removed from the body by renal excretion through the glomeruli,[1] and they are virtually useless as plasma expanders,[2] since any effect obtained will be nearly as transient as if physiological saline had been administered. Material with high molecular weight has other disadvantages, especially evident because large concentrations are needed to produce colloid osmotic pressures equivalent to that of plasma (30–40 cm. of water). High molecular weight solutions are unduly viscous. They may form precipitates with plasma constituents, especially with fibrinogen[3]; they are deposited in the reticulo-endothelial system[2,4]; and they tend to aggregate red blood corpuscles, as shown by a raised erythrocyte sedimentation rate. These last two effects are probably more marked in solutions of equivalent molecular size with polyvinyl pyrrolidone than with dextran.

For use as plasma expanders, then, colloid solutions of intermediate molecular size are required—perhaps of the order of 70,000 to 100,000 for dextran, and somewhat smaller for polyvinyl pyrrolidone. Attention may also have to be directed to the molecular shape of the material. This varies in dextrans from different sources according to the nature of the linkages between its component glucose units. Medical men must choose the material to give their patients, and this implies manufacture to specification, as was adopted temporarily in the early clinical trials of dextran in Britain.[5] Suitable specifications and legal control of the composition of plasma expanders are therefore required before they can be recommended unreservedly and full advantage taken of their sphere of usefulness. This does not (and cannot) include their substitution for blood in the treatment of severe haemorrhage or anaemia. More blood donors still are needed.

MEDICAL LIBRARIANS IN CONGRESS

London is unequalled for its wealth of medical libraries: some of the most important collections in the world are contained within a small area—the libraries of the Royal Colleges, of the Royal Society of Medicine, of the B.M.A., of the London School of Hygiene, and the Wellcome Foundation's famous historical collection. Appropriately, therefore, the First International Congress on Medical Librarianship is to be held in London, from July 20 to 25. Sir Cecil Wakeley, P.R.C.S., is the president of the Congress, and he will be supported by thirty-eight vice-presidents, representing the chief medical libraries of the world, universities, and other organizations. Exhibitions to be held in connexion with the Congress are of medical periodicals (in the Old Library of B.M.A. House), of medical books and equipment (in the Gymnasium of University College), of the U.S. Armed Forces Medical Library (in the auditorium of the Wellcome Research Institution), and of the history of medical libraries and of medical bibliography (in the Wellcome Historical Medical Museum).

Sir Cecil Wakeley, in a presidential message to the Congress, quotes Osler's warning that "to study the phenomena of disease without books is to sail an uncharted sea," and he aptly continues the simile by emphasizing the needs not only for charts but also for pilots, among which medical librarians can count themselves. Pilots, of course, should be carefully trained, and one of the subjects to be discussed at the Congress is the education and training for medical librarianship. At present Britain is the only country in which medical librarians qualify as such by special examinations. Two sessions of the Congress will be given up to a symposium on the role of the medical librarian in the world to-day.

Among the other subjects to be debated are international co-operation and aids to the current indexing of medical literature—a matter of topical importance, since the existing indexes are falling behindhand. By discussing their common problems at this Congress and by fostering the spirit of international co-operation, medical librarians will be increasing their already great contribution to the spread of scientific learning throughout the world.

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REFRESHER COURSE FOR GENERAL PRACTITIONERS

LEUCORRHOEA

BY

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Whiteness is not a common feature of the abnormal discharges from the vagina, and so the word "leucorrhoea" is being used less and less : it is being replaced by the more widely applicable phrase "vaginal discharge," which covers all varieties of discharge regardless of colour, though usually excluding those that are blood-stained. The symptom is common ; it occurs at all ages and is of widely differing significance.

Bacteriology

A distinction must be drawn between the flora of the vulva and vestibule and that of the vagina. At birth the vulva and vestibule are usually sterile, but this state of affairs does not last long : within a few hours organisms reach the area. Their type depends largely on those present in the immediate environment ; provided this is clean, pathogenic bacteria in harmful concentration will be absent.

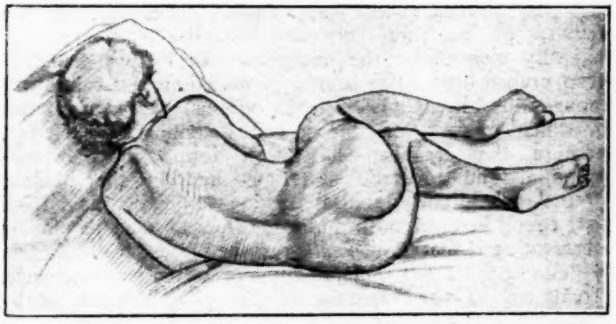
During the mother's pregnancy the foetal vagina is under the influence of the maternal oestrogens, and at birth therefore its epithelium is well stratified and the cells contain glycogen. Within 12 to 24 hours of birth Döderlein's bacillus makes its appearance and remains for about two weeks, until the effect of the maternal oestrogen has worn off. This bacillus, assisted by enzyme activity, is thought to break down the glycogen in the vaginal cells into lactic and other acids in lesser amounts, which together have a powerful bactericidal action. By the end of the second week of life the vagina is probably once again sterile, and it normally remains so in infancy and childhood. Another factor in keeping the vagina free of pathogenic bacteria during this period may be the anatomical arrangement : the walls of the vagina are in close apposition and the introitus is so nearly closed by the hymen that the passage of harmful organisms upwards from the vulva is unlikely.

During the reproductive years of life the bacterial flora is mixed, and pathogenic bacteria may be present, particularly in the lower one-third of the vagina. But they should not survive long, being inhibited in their growth by the vaginal acidity (*p*H 4–5.5). It has been estimated that a concentration of lactic acid of 1% may be present during these years. The vaginal acidity, which is so important in maintaining vaginal health, is temporarily neutralized by the menstrual flow, and this accounts for the tendency of infections of the vagina to return or relapse after each period.

Examination of the Patient

From all patients complaining of vaginal discharge a careful history must first be taken to obtain as much information as possible about the time and mode of onset ; its quantity, colour, and consistency ; whether it is irritating, offensive, or blood-stained ; and any other special features. Then examination should be carried out in a good light. After preliminary examination of the abdomen and any general examination that seems necessary, the patient should be made to lie comfortably on her back with her thighs drawn up and separated ; the labia are then parted, and the vaginal introitus is examined for the presence of discharge, signs of inflammation, ulceration, or oedema or other swellings. The urethral orifice should be swabbed clean with saline ; if there is any suggestion of urethritis the urethra should be gently "milked" downwards with the finger on the anterior vaginal wall ; if it is possible to express pus from the urethra a swab must be sent for bacteriological examination : pus can never be expressed from the urethra in a simple case of vaginitis ; it always means that there is some other condition present. The patient should then be turned on her side with her thighs drawn up, the upper one slightly more so than the lower one (see Fig.), and a lubricated Sims speculum gently inserted into the vagina.

If a discharge is seen a specimen diluted with saline should be inspected under the microscope for trichomonas or the spores and hyphae of vaginal thrush. The discharge is then removed with a swab on sponge-holding forceps, and the vaginal walls are carefully inspected for redness, signs of abrasion, ulceration, or other abnormality. The



Position for examination with a Sims speculum. A lower pillow or even no pillow might be better.

cervix is next inspected for erosion and evidence of cervicitis, and any excess of cervical mucus noted. Sometimes it is helpful to turn the patient into the knee–chest position, because, with the Sims speculum in the vagina and the patient in this position, the vagina balloons out, and a very clear view of the vaginal walls may be obtained. Finally, an ordinary bimanual examination should be performed to exclude disease of the pelvic organs.

In most cases this examination will give as much information as is required to find out the cause of a vaginal discharge. If the findings are equivocal specialist opinion should be sought, as special culture methods may be necessary.

Vaginal Discharge before Puberty

Vaginal discharge before puberty is most commonly a sign of infection, seldom localized to the vagina, more usually taking the form of a vulvo-vaginitis : any of the pathogenic bacteria may be responsible. The vulva and vaginal introitus are red, swollen, and oedematous, depending on the severity of the infection. There may be purulent discharge, in which case it should be possible to obtain some on a swab for immediate culture. Treatment with one of the sulphonamides or other appropriate antibiotics is usually quickly effective: daily baths with gentle washing and drying are also indicated. In resistant cases oestrogens (ethinyl oestradiol or stilboestrol) should be given by mouth, the dose being appropriate to age. For a child of 6 a daily dose of stilboestrol 0.5 mg. should be sufficient.

Another cause for discharge in childhood and infancy is a foreign body in the vagina. This may sometimes be

seen sticking in the introitus, when it may be readily removed. If the foreign body is well in the vagina, recognition is much more difficult, though it may be possible to feel it with a little finger in the rectum. For removal, admission to hospital and examination under anaesthesia with tiny specula (Kelly's cystoscope may be useful) is usually required.

Vaginal Discharge During the Child-bearing Years

Discharge at this time is fairly common and generally results from infection of the vagina or cervix. The two common forms of vaginitis are those due to *Trichomonas vaginalis* and to the fungus *Candida albicans*. Cervicitis is usually the result of lacerations at childbirth, with infection and failure of involution leading to chronic hypertrophy of the cervix, and thus to blockage of the cervical mucus-secreting glands with the formation of visible cysts, known as Nabothian follicles.

Trichomonas Vaginitis.—*T. vaginalis* is an oval flagellate with axostyle and undulating membrane; it is found in great numbers in the vaginal secretion in certain forms of vaginitis. The discharge in these cases is offensive and may cause a burning sensation: dyspareunia, dysuria, and frequency of micturition are other symptoms. In appearance the discharge is yellowish, watery, and slightly frothy. The vagina may be very tender: it looks inflamed, and widespread discrete red spots may be seen, giving the surface a strawberry-like appearance. Because of the activity of its three or four flagellae the organism is easily seen under the microscope in a fresh hanging-drop preparation. The source of infection is not known: though the disease is seen in virgins, there are cases in which transmission during coitus cannot be excluded, because the organism has been found in the subpreputial and prostatic secretions and in the bladder of the male. The organism causing vaginitis differs from that found in the mouth and large bowel. One perplexing observation is that *T. vaginalis* may be present in the vagina without causing any inflammation or other inconvenience. Treatment of the vaginitis, in the first instance, is by pessaries, such as those containing acetarsol or silver picrate. The patient should be told to insert one or two pessaries each night between two periods, and thereafter daily for the week immediately following the next two periods. This will cure most cases. Alternatively, antiseptics may be injected as a thick cream into the vagina by means of special applicators. Douches are of little value in the treatment of vaginitis: they may, however, be prescribed two or three times a week as a method of cleansing the vagina between treatments. Salt solution, one teaspoonful of salt to the pint (570 ml.), should then be used. For the few cases which are not cured, vaginal cleansing, drying, and powdering twice a week is required, using acetarsol or silver picrate powder. Insufflation of the vagina with antiseptic powder must *never* be carried out in pregnancy, because of the risk of fatal air-embolism. In resistant cases the possibility of reinfection by the husband should be considered.

Vaginal Thrush.—This form of vaginitis is particularly common during pregnancy and causes much local irritation. The findings are striking: the vaginal walls are covered with a thick white curd-like matter that adheres to the skin. Confirmation of the diagnosis is made by finding the characteristic spores and hyphae on microscopy. The urine in such cases should be particularly tested for sugar. Treatment comprises, first, vaginal cleansing under vision, with soap or detergent and water, until all the matter has been removed; and, secondly, antiseptic measures. The cleansing gives the patient immediate relief, and should be repeated twice a week. Thereafter the vagina, vestibule, and vulva are painted carefully and completely two or three times a week for two weeks with 1% gentian violet in water or 1% gentian violet in equal parts of spirit and water, care being taken that no vaginal folds are overlooked. Alternatively, chlorophenesin ("mycil") pessaries may be advised. In resistant cases subclinical diabetes should be excluded by a sugar-tolerance curve.

Cervical Discharges

Cervical erosion is recognized by finding a circular area of velvety redness around the external os. This appearance results from the downgrowth of columnar epithelium from the cervical canal. If, in addition, there is overgrowth of the columnar epithelium the erosion is thrown into folds and may be called papillary. The condition is seen in virgin women and in women who have not borne children, and its cause is then unknown: in parous women infection at childbirth is probably the main factor, and the erosion is seldom seen without some cervicitis.

Chronic cervicitis produces a sticky discharge, not usually irritating or offensive unless there is some superadded vaginitis. It may also be associated with a number of other symptoms, particularly lower abdominal aching and backache, which probably originate from the tense, blocked cervical glands. The general health may be impaired. There may also be sterility, because the purulent cervical discharge is inimical to the spermatozoa.

The cervix in such cases is hypertrophied, lacerated, and often everted. The columnar epithelium of the canal may be exposed and may have replaced the squamous epithelium around the external os as in erosion. Mucoid material may be seen in the os, and when it is lifted away with forceps its stickiness is at once apparent. There may be an associated parametritis, when the woman may complain of pelvic pain, backache, and dyspareunia; then pain on moving the cervix is an important sign. Bacteriological examination of cervical discharges is necessary only if there is an associated urethritis or Bartholinitis, or if the condition does not respond to treatment; then specialist facilities are required because of the uncertainty in excluding gonococcal infection by smears and culture methods alone, and because of the advisability of blood tests.

Cervicitis may be materially improved by superficial linear cauterization of the cervix in the out-patient department, the anterior lip being treated one week and the posterior lip the next; but symptoms are unlikely to be completely relieved, at least in a severe case, until deep cauterization with electric hot-point, diathermy coagulation, or excision with knife or diathermy of a substantial part of the hypertrophied cervix has been carried out; for these latter procedures admission to hospital or nursing-home and anaesthesia are required. Treatment in this way is effective; there are few complications and little risk. The most troublesome complication is secondary haemorrhage occurring about the end of the second week. This is treated by morphine and rest if the bleeding is slight, and by a firm vaginal pack if bleeding is severe. Very occasionally a widespread pelvic infection flares up after cervical cauterization. In women over the age of 40 amputation of the cervix or even hysterectomy may be preferred.

The prevention of cervicitis is an aspect of intrapartum and post-partum care which tends to be neglected. During labour every care must be taken to prevent infection of the mother, by strict aseptic and antiseptic techniques and by keeping her away from the sources of infection. Should infection occur it must be treated adequately. When the woman is examined a month or so after delivery the examination should include a careful assessment of the state of the cervix and thorough speculum examination in a good light so that any cervical faults may be recognized and treated without delay.

Post-menopausal Discharges

After the menopause the lack of ovarian secretion leads to a partial atrophy of the vaginal epithelium, which together with lack of acidity at this time may allow infection to occur. A thin watery discharge results which may be blood-stained, and the vagina shows a widespread punctate red

mottling. In such cases preliminary curettage, possibly cervix biopsy, and examination under anaesthesia are usually required to exclude genital cancer. Treatment of the vaginitis is first by oestrogen pessaries, one twice daily for two to three weeks, reserving stilboestrol 0.5 mg., or ethinyl oestradiol, 0.05 mg., daily by mouth, together with sulphonamides or antibiotics locally or parenterally, for resistant cases. Treatment with oestrogen by mouth should not be continued for more than 7 to 10 days at a time if the likelihood of oestrogen-withdrawal bleeding is to be kept to a minimum. Pessary treatment is less likely to cause such bleeding.

Also after the menopause are to be seen the discharges caused by retained and neglected pessaries and by other foreign bodies. After removal of the irritant the discharge usually clears up quickly unless some permanent damage has resulted.

After the menopause and after surgical procedures on the cervix there may be some cervical stenosis leading to accummulation of fluid or pus in the uterus, forming a hydrometra or pyometra. This may discharge suddenly or intermittently. Examination under anaesthesia and dilatation and curettage are required in such cases to establish the diagnosis, to promote drainage, and to exclude associated cancer.

Miscellaneous Causes of Discharge

Every now and then a woman is seen with a severe vaginitis which is being maintained by treatment. Douching with antiseptics can cause a severe vaginitis either because the antiseptic remains on the skin in high concentration after the water has evaporated or, more likely, because of skin sensitivity; the daily wearing of a tampon can also cause much local irritation. To stop all local applications is the obvious first treatment in such cases; often no other therapy is required.

More troublesome is the occasional patient who has a vaginitis, often of unknown aetiology, in which the epithelium in some part of the vagina, perhaps at the vault, is seriously devitalized, being thin, atrophic, and often with great loss of mobility. The most that can be done in such cases is to search diligently for the cause, while trying by the judicious use of oestrogens locally and tonic measures generally to improve the patient's healing powers. Meantime temporary avoidance of coitus is desirable to encourage healing.

It is worth bearing in mind that watery discharges may be urinary in origin. If dating from a difficult confinement or operation, there may be a tiny vesico-vaginal fistula, perhaps with a sinuous tract and only discharging intermittently. Closely allied are the very rare cases in which a cyst of Wolffian duct origin has an external opening and discharges a small amount of fluid. Perineal sinuses, stitch abscesses, and tiny rectal fistulae can all cause vaginal discharge. The appropriate surgical treatment is required for all such cases.

A watery blood-stained discharge is an important sign of early carcinoma of the genital tract, especially carcinoma of the cervix and of the corpus uteri. If there is any suspicion of these diseases, careful examination under anaesthesia, biopsy of the cervix, and dilatation and curettage must be carried out without delay.

Next Refresher Course Article.—"Scrotal Swellings," by Mr. R. J. McNeill Love.

Refresher Course Book.—The first collection of articles of this series (fully revised) are available as a book containing 55 chapters, price 25s. Copies may be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

BRITISH EMPIRE CANCER CAMPAIGN

REPORT FOR 1952

The thirteenth annual report of the British Empire Cancer Campaign, covering the year 1952, is an impressive volume of over 400 pages. It records the results of work in many centres in Britain; deals briefly with cancer research in Canada, New Zealand, Australia, and South Africa; and describes the researches of individual investigators supported by the Campaign, of Campaign Fellows, and of Campaign Exchange Fellows. In 1952 income from donations, collection, and legacies was £318,773, the highest figure so far attained. The total is £59,000 above the previous year, mainly owing to a large increase from legacies, which amounted to £138,416. In addition £19,393 was received from investments. The Campaign spent £221,439 on cancer research, £36,623 on appeals and publicity, and £8,162 on administration. There was a balance of £88,910 of income over expenditure at the end of the year.

The Campaign is attacking cancer on a wide front. This is evident from the admirable summary, by Lord Horder and Sir Heneage Ogilvie, of the work supported. There are sections on experimental and clinical carcinogenesis, hormones, the biochemistry of growth, tumour viruses, experimental chemotherapy, radiation chemistry and radiobiology, radiotherapy, and clinical pathology.

Clinical Pointers

Technical advances in radiotherapy which make it more effective, yet at the same time less unpleasant for the patient, are a major contribution to cancer research. There is, for instance, the use of very high-powered radiotherapy units. As long as 15 years ago a million-volt machine was being used in Britain, and to-day there are several operating at 2 MeV. Now, apparently, with the installation of *x*-ray equipment operating at voltages up to 30 MeV, we are about to enter what is likely to be the last phase of this line of advance. To reach this stage a great deal of painstaking physical and biological research has been necessary. At the Middlesex Hospital the much less costly "rotational therapy" method of delivering a large radiation dose to deep-seated lesions is being investigated, and the results appear promising. Work at Cambridge suggests that the combination of a chemical radiosensitizer ("synkavit") with conventional *x*-ray therapy may prolong the lives of those with inoperable bronchial carcinoma. At many centres the possibilities of radioactive isotopes are being eagerly explored. In contrast with the success of physical methods in treating cancer, trials of new chemotherapeutic substances have been less fruitful; nor has the work on hormones yielded any new lines of treatment for immediate application.

What may be termed environmental cancers have received their full measure of study. A suggestion that coal smoke and tobacco smoking may act together after the manner of a carcinogen and a co-carcinogen in causing lung cancer is being checked by studying the amount of carbon in the lungs and bronchial glands. Questions such as, Why is lung cancer rare in coal-miners? Why is it common in London, in both sexes? are being examined by statistical methods. Other experiments aim at isolating the products of cigarette smoke with a view to testing their carcinogenic activity in animals. Bladder cancer in dye-workers has been the subject of a four-year field study and of a report to the Association of British Chemical Manufacturers. Some interesting findings have emerged: each individual carcinogen has a characteristic induction time, and the age at which tumours appear depends on when exposure began; and, although incidence may depend on severity of exposure, the induction time is not affected by this. In parallel with the field work, the carcinogenic properties of the aromatic amines have been studied in the laboratory. Among other things, this may help in deciding which of them are too dangerous for industrial use. With a similar object, the carcinogenic activity of crude oils and their fractions has

been assessed. Several Kuwait and Lagunillas sub-fractions are strongly carcinogenic in rabbits.

Among other observations of direct clinical use is the recognition of the value of serial biopsies during radiological treatment of carcinoma of the cervix (this permits the rapid recognition of radio-resistant cases which can then be treated surgically), and of restricting salt intake after uretero-colic anastomosis for bladder tumours (this reduces the mortality from disordered metabolism). Another study defines the place of local *versus* widespread excision in the treatment of malignant rectal polyps.

Radioactive cobalt dust was found to have been leaking from the radio-cobalt units in Leeds and Sheffield, and radioactivity was detected in their operators. However, the amounts absorbed were well within the safety range, and the faults in the machines have been dealt with.

Fundamental Research

It is a truism that, when dealing with a really stubborn problem, the quickest solution is not always the most direct. This is certainly so in medical research, and much of the report of the British Empire Cancer Campaign is concerned with fundamental research. From a host of such studies it is possible to pick out only a few for remark. Some of the most interesting work is on the way in which chromosomal aberrations take place. By applying a chemical mutagen to the root-tip cells of beans it has been possible to observe what happens. This has led to an entirely new interpretation of chromosomal aberrations: namely, that chromosome breakage and reunion are simultaneous, the event being similar in nature to chiasma formation in meiosis. In the words of the report, "There is no need to emphasize the importance which would attach to any correlation between mutagenesis, carcinogenesis, and something akin to the physiological process of meiosis, rather than through a more random mechanism of damage and repair by chance."

Anything that adds to our knowledge of the processes of normal growth may throw light on the disorded growth of cancer: hence the interest of the observation that in the chick embryo ascorbic acid synthesis is related to the rate of growth. The next step, which is being taken, is to see whether this applies to tumour tissue also.

Lastly, from this mine of material, one experiment may be selected for its technical virtuosity. It has proved possible to take the nucleus from one amoeba and exchange it with that of another. This remarkable feat has been used to study the effects of nitrogen mustard and *x* rays on nucleus and cytoplasm separately. The results show that direct damage is done to both nucleus and cytoplasm, although the nucleus is the rather more vulnerable of the two.

Pedestrians over 60 are involved in a high proportion of road accidents, and, as the ratio of people in the higher age groups is increasing, their safety on the roads is becoming a greater problem. In March the Pedestrians' Association held a conference on this subject, and the report of this meeting has now been published by the association. Road accidents are often due to the inability of the elderly to adapt themselves to the speed and volume of modern traffic. The report recommends that local authorities and road safety committees should, where necessary, provide special facilities for old persons to cross the road. Propaganda should be directed to drivers, many of whom make insufficient allowance for the limitations of the elderly. Conductors of public vehicles should show special consideration for elderly passengers. The old people themselves should be given advice about road usage, and clergy and social workers among old people should use their opportunities to do this. Lame and infirm persons should, if possible, be accompanied on the roads; risks of accidents to them could be minimized by the organization of a rota of neighbours, social workers, etc., to do their shopping. The report costs 1s. (by post 1s. 2d.), and is obtainable from Mitre House, 44–45, Fleet Street, London, E.C.4.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Male Pseudohermaphroditism

SIR,—I have read with the greatest interest the account by Drs. D. C. Beatty, C. J. Champ, and G. I. M. Swyer of "A Case of Male Pseudohermaphroditism" (*Journal*, June 20, p. 1369), since a case which conforms fairly closely to the clinical picture which they describe has come under my own observation, and forms the subject of a chapter ("Features in the Analysis of a Patient with a Physical Genital Abnormality") in my recent book.[1] My interest in the case was primarily psychiatric, the individual in question having been referred to me by "her" family doctor for psychotherapy on account of symptoms of anxiety and periodic depression. Accordingly, my reference to the physical aspects of the case is only incidental—which is perhaps unfortunate from the standpoint of general medicine, since I understand that only a few such cases have been described in the literature. It is also unfortunate from this standpoint that I found it necessary to withhold certain interesting data from my account and to leave others intentionally vague for reasons of discretion. My account is subject to further limitations in consequence of the fact that, although it was not published until 1952, it was written in 1930 for a meeting of the British Psycho-Analytical Society on January 21, 1931; for at that time knowledge regarding the sex hormones was less advanced than it is to-day, and laboratory facilities for their investigation were comparatively undeveloped. Also, I did not feel it justifiable to seek confirmation of the nature of the gonads by subjecting the patient to exploratory surgical intervention solely in the interests of scientific curiosity, especially since the effect of such intervention and of discovery of the data thereby revealed might well have inflicted a psychological trauma upon the patient, whose mental equilibrium was already precarious. The interested reader will perhaps desire to refer to my published account; but I take the opportunity to draw attention to certain of the data which it contains.

The patient to whom I refer had always been regarded as female, even after the discovery of her abnormality by her family doctor, whose introductory letter included the following statement: "She appeared to be a perfectly normal child until she reached the age of puberty. She began then to grow unduly tall, but did not menstruate, but kept perfectly well. When she was about 20 I was consulted, and made an examination. I found . . . only a pin-head opening as a vagina which led nowhere. As she felt perfectly well, nothing further was done."

Accepting the doctor's account, I took no steps to initiate a more detailed physical investigation before proceeding with psychotherapeutic treatment. As treatment proceeded, however, I began to entertain doubts not only regarding the adequacy of his account, but also regarding the sex to which "she" properly belonged. Accordingly, I arranged for the patient to be examined by a distinguished gynaecologist, who reported it as his impression that the case was one of male pseudohermaphroditism, and who described his findings in the following terms: "The general development is strongly masculine; the chest is very broad, but the mammary development is, if anything, more suggestive of the female type in that the tissue is soft and slightly dependent. The pubic hair is normal in its distribution for the female, and the more superficial organs are quite definitely female—namely, labia, mons, clitoris, vestibule, and urethra. The hymen is completely closed, and is represented by a series of small bands crossing the site of the normal depression. Rectal examination was not easy, but . . . no cervix or uterine body was made out. These, under ordinary circumstances, are usually made out with perfect ease by this route. At the same time the examination was not sufficiently complete to exclude the presence of an imperfectly developed organ. The general impression which I have formed is that we are dealing with a condition of essential masculinity with the presence of male gonads accompanied by secondary characters of a female type."

It may be added that, in spite of his diagnosis, the gynaecologist agreed with my opinion that it would be inadvisable to acquaint the patient with the nature of his findings. Doubts were, however, subsequently cast upon the diagnosis when a specimen of the patient's urine was examined for oestrin and gonadotropic content, and reported upon as follows: "Oestrin—at least 20 mouse units per 24 hours. Gonadotropic content—less than 100 mouse units of follicular maturation hormone per 24 hours. These excretion results are similar to those usually obtained in a female subject, and the oestrin excretion is higher than would be expected in a male. The results suggest the presence of female secretory gonads."

In the light of this report I considered it all the more desirable to continue, for practical purposes at any rate, to regard the patient as a female.

The case in question differs interestingly from that described by Beatty, Champ, and Swyer in the facts that pubic hair was present and that the patient was abnormally tall (about 6 ft. 4 in. (1.93 m.). Another interesting feature was that during adolescence she was subject to recurrent rectal haemorrhages which lent themselves to interpretation in terms of vicarious menstruation, and which were actually mistaken for proper menstrual periods. These were followed later in life by periodical bouts of epistaxis, which lent themselves to a similar interpretation. It is also a striking fact that, while under my observation, she always spoke quite spontaneously of her periodic attacks of depression as "being unwell," and would also speak of "missing a turn" when an attack was deferred for longer than usual. The case conformed to the description of Beatty, Champ, and Swyer in that she had a definitely female mentality and displayed no evidence of Lesbian characteristics; and it may be added that her libido was highly developed towards men, and that men seemed to find her singularly attractive.

In conclusion it is of interest to record that an identical abnormality was present in several of her numerous sisters, the remainder of whom were normal women, married, and the mothers of children.—I am, etc.,

Edinburgh. W. RONALD D. FAIRBAIRN.

REFERENCE

[1] *Psychoanalytic Studies of the Personality*, 1952, p. 197. Tavistock Publications, Ltd., London.

Mean Body Weight, Food Intake, and Temperature

SIR,—Although Alice's consumption of cake and mushroom was undoubtedly responsible for some of the variations in her size, and hence presumably weight, it was, significantly, the White Rabbit's fan that she dropped hastily to avoid shrinking away altogether. The fact that the fan was overlooked when its owner discovered Alice is no excuse for it to be forgotten in preoccupation with other matters this side of the rabbit hole. In the discussion of the valuable paper by Mr. J. M. Harries and Miss D. F. Hollingsworth (*Journal*, January 10, p. 75) little reference was made to non-dietary factors, other than activity, affecting body weight: the suggestion therefore that weight data can be used as an "index of inadequacy in food supplies" deserves some comment.

The closeness of the demonstrated weight-calorie relationship is paralleled by that between weight and mean temperature of the month in which it was recorded. The correlation coefficients for the whole series are respectively $r_{cw} = +0.612$, $r_{tw} = -0.730$, both highly significant; these may be obtained from the analysis, given in the table, of variance and co-variance, calculations permissible since serial correlations in the weight series used were not significant and since there was no reason to assume serial correlations in the independent variates. That these correlations were independent of each other is shown by the partial correlation coefficients ($r_{cw.t} = +0.586$, $r_{tw.c} = -0.714$). The temperature factor therefore should also be considered in assessment of the adequacy of food supplies from body weight.

Several points of interest emerge from the figures in this table. Limitations of the data may well account for the insignificant contributions by temperature and calories to the small residual sum of squares for weight. The calorie effect predominates in the longer term weight fluctuations and contributes little to the seasonal variations, while it is in the latter that the temperature effect is most marked. Thus it might appear that the state of food supply in Britain is indicated by mean body weight if this is observed over a long period—long enough, that is, for temperature fluctuations to be cancelled out. However, caution is still necessary, since differences in weight from year to year remain highly significant after allowance is made for calorie intake, both alone and in combination with temperature. Some further influence thus appears to operate on long-period variations in weight, and hence not all such can be used to diagnose dietary adequacy or inadequacy. Not all of Alice's metamorphoses were occasioned by what she ate and by the White Rabbit's fan.

Analysis of Variance and Co-variance of Mean Weight (Males), Temperature, and Calorie Intake

Source	Degrees of Freedom	Sums of Squares			Sums of Products		
		Weight	Temperature	Calories	Wt./Temp.	Temp./Cal.	Wt./Cal.
Years ..	5	8·6174	37·53	51,854	−4·225	−435·4	+514·78
Quarters	3	11·2815	1,720·68	9,918	−136·664	−3,173·9	+286·86
Residual	15	1·1067	74·68	27,369	−2·381	−455·2	+35·36
Total	23	21·0056	1,832·89	89,141	−143·270	−4,064·5	+837·00

The writer wishes to acknowledge his indebtedness to Mr. M. H. Quenouille, of the Institute of Statistics, Oxford, who advised upon statistical procedures, and to Mr. Harries and Miss Hollingsworth, of the Ministry of Food, who made available their data for further examination, which was prompted not by any spirit of unappreciative criticism but rather by the wider implications of their work.—I am, etc.,

Oxford. D. F. ROBERTS.

Peptic Ulcer in Women

SIR,—Mr. D. H. Clark's article on peptic ulcer in women (*Journal*, June 6, p. 1254) essentially confirms the findings of previous authors and establishes the absence or disappearance of peptic ulcer symptoms during pregnancy as the most impressively unequivocal coefficient in the natural history of this much studied and as yet incompletely understood condition.

In Mr. Clark's series of 400 women over the age of 21 with histories of peptic ulceration, 204 of whom had reached the menopause, only 118 had pregnancies, and it would be interesting to know how this proportion compares with a similar but unselected group of women in the same town. Should the incidence of pregnancies in Mr. Clark's series be significantly lower than in the unselected sample, this would enhance the importance of his observations on the reverse aspect of the correlation—namely, the frequency of pregnancy toxicoses in sufferers from peptic ulceration in whom the ulcer symptoms persisted or recurred during pregnancy. The possibility then arises of an abnormality of the endocrine secretions being the common factor underlying peptic ulceration, some cases of pregnancy toxicosis, and at least one circumscribed type of sterility in women. The data suggest strongly a correlation between the secretion of some of the sex hormones and the inhibition of the periodicity of peptic ulceration and emphasize *inter alia* the need to study the curious and often dramatic action of gonadotrophic hormones of placental origin on the symptoms of peptic ulcer patients. This does not imply that gonadotrophic hormone produced during pregnancy has a specific effect or even any direct effect upon ulceration, but only indicates that it is involved in some manner, a subject which I have recently discussed elsewhere (*Lancet*, 1953, 1, 1000).—I am, etc.,

London, W.1. T. CSATO.

Intravenous Barbiturates for Drunkenness

SIR,—Dr. Peter Nobes's comments (*Journal*, April 11, p. 836) to my letter on this subject (*Journal*, January 17, p. 163) call for a reply in defence of my procedure in dealing with such cases.

Dr. Nobes theorizes on what might happen if my procedure was adopted for "obstreperous drunks," but surely such complications as "silent regurgitation" and "glottic spasm" are no more a danger here than in any of the emergency cases that receive a similar dose of any intravenous barbiturate. Moreover, I think I am right in saying that when the stage of obstreperous behaviour is reached

such cases have an empty stomach, either from an earlier stage of vomiting or from having digested what was already there. However, I wonder if Dr. Nobes has ever tried to wash out the stomach of an obstreperous drunk.

I do not think that the fact of my series of cases coming through without a mishap was just pure luck on my part. None of them developed a venous thrombosis with the 10% solution either.—I am, etc.,

Tumatumari, British Guiana. A. M. BARTLEY.

Amphetamine

SIR,—The element of historical interest introduced in your leading article "Mr. Macleod on the Drug Bill" (*Journal*, June 20, p. 1380) is somewhat misleading. The volatile amine—β-phenylisopropylamine (amphetamine)—was first prepared from phenylmethylacrylic acid by Edeleano in 1887.[1] In 1910 Barger and Dale,[2] during a pharmacological examination of aromatic amines, described this drug as a member of a group of similar substances to which they gave the name "sympathomimetic." For 20 years thereafter no attention was paid to this compound, the interest of investigators being centred on ephedrine.

Amphetamine sulphate ("benzedrine") was first prepared and investigated by G. A. Alles in 1927[3] also in the course of a search for a compound better than ephedrine. He discovered its stimulating effect on the central nervous system and suggested that this might have therapeutic value. At that time attention was focused on the peripheral effects of the amine, and through the pioneer work of Messrs. Smith, Kline, and French Laboratories, of Philadelphia, the base was introduced to the medical world in 1932 as the first volatile nasal vasoconstrictor. However, they also started an extensive pharmacological investigation to follow up the observations made by Alles on the systemic action of the drug, and in 1935 Prinzmetal and Bloomberg[4] were able to report on the value of amphetamine sulphate in narcolepsy—a condition in which it is now regarded as diagnostic and specific. Since that date the value of this drug has been confirmed in a wide range of clinical conditions.

The anorexigenic properties of the amphetamines were first reported as a side reaction when the drug was used for its psychic effects[5] and amphetamine sulphate found some use as an aid in the treatment of overweight. However, as a result of further work the dextro-isomer—dexamphetamine sulphate ("dexedrine")—was isolated and made available some 10 years later, and was found to be preferable in this and a number of other conditions. It thus appears that this valuable drug, although known since 1887, was ignored until its potentialities were explored and developed by a pharmaceutical house.

This is an example of the special contribution made by pharmaceutical manufacturers to medical practice—the way in which they are able to develop and extend a new discovery and greatly reduce the time interval between laboratory work and its clinical application.—I am, etc.,

London, S.E.5. T. C. BLACK,
Menley and James, Ltd.

REFERENCES

1. *Ber. dtsch. chem. Ges.*, 1887, **20**, 616.
2. *J. Physiol. (Lond.)*, 1910, **41**, 19.
3. *J. Pharmacol.*, 1927, **32**, 121.
4. *J. Amer. med. Ass.*, 1935, **105**, 2051.
5. Nathanson, M. H., ibid., 1937, **108**, 528.

Medical Auxiliaries

SIR,—I do not think that those who advocate freedom for study and work for all will agree with the opinion expressed in your leading article on medical auxiliaries (*Journal*, June 6, p. 1267).

The decision of the Minister of Health to give equal rights to the three associations of physiotherapists and not to accept monopoly in favour of the Chartered Society, far from being a "meagre conclusion," is, in fact, an act of justice and statesmanship. I am the first to recognize the good work done by the Chartered Society, but it is common knowledge that the Physiotherapists Association and the Faculty of Physiotherapists include at least equally well trained and skilled physiotherapists who are doing excellent work. To refuse these keen workers hospital facilities to study, and to bar them from hospital employment, would be an arbitrary and unjustified measure. As the monopoly in favour of the Chartered Society has been proposed by a committee composed, apart from the president and two Government officials, by six other members all connected with the Chartered Society, it is not astonishing that the Government demanded a wider inquiry which resulted in the declaration of the Minister of Health: "Fairness to all societies concerned."

I cannot understand why this decision of the Minister has been considered as a criticism of the Cope report. This report represents a painstaking work in which general directions are proposed for medical auxiliaries. It is unfortunate that this question of monopoly has cropped up, but surely an amicable settlement of this vexed problem can be reached.

We are in great need of good physiotherapists, but for that we must avoid monopolies and exclusiveness. We must open wide the portals of the hospitals to all those wishing to devote themselves to that branch of the healing art, demanding from them not a label of any particular association but keenness, hard work, and skill.—I am, etc.,

London, W.1. A. P. CAWADIAS.

Children in Hospital

SIR,—It is believed that the Ministry is encouraging an increase of visiting at children's hospitals. It would seem that this is related to the annotation (*Journal*, March 14, p. 609) in which daily visiting at Great Ormond Street Hospital for Sick Children was favourably reported. I have nothing to say on the medical or administrative angle of this matter with regard to a short-term hospital, but with regard to the long-stay orthopaedic hospital I think frequent visiting is distinctly detrimental to the children. It should be realized that in long-stay hospitals the child has to make an entirely new adjustment to a life which is likely to continue for two or more years. Frequent visiting delays or utterly prevents this adjustment by reminding the child constantly of home life. It is very noticeable that new arrivals are upset by the first few visiting days which they experience, and there is little doubt that the quickest, and possibly the kindest, way of bringing about adjustment would be the prohibiting of visiting altogether, or at least during the first six weeks of admission—as is done at most boarding schools.

At this hospital we have endeavoured to achieve a compromise by fortnightly visiting, and we find that after the first six weeks the children look forward to visiting day with good cheer and manage to keep in touch with their parents in this way without being gravely upset when the visit closes. The opinion has been expressed elsewhere that infections are not introduced to children's hospitals on visiting days. It has been noticeable nevertheless that the majority of new infections and dietetic upsets are referable to the past visiting day.

A further consideration which should not be neglected with regard to visiting at long-stay hospitals is the hardship inflicted on parents who naturally feel they must visit their children as often as possible. The majority can and do manage a long journey every alternate week-end for months or years, at very considerable sacrifice. Many beggar themselves by bringing a multitude of toys on each occasion—toys which are usually broken within two or three days of the visit. There remains, however, a proportion of parents who absolutely cannot manage to visit as frequently as the rest and therefore their little one finds itself isolated on visiting days. Visiting permitted more frequently than fortnightly would enhance the hardship to the parents and increase the discrimination between visited and neglected children which the unfortunate children are incapable of understanding and therefore of tolerating.

This problem is a delicate one, and no effort should be made by the administrators to interfere with what is primarily a medical decision, which must be governed by individual hospital circumstances. It is also worth remembering that it is foolish to abandon a tried and reasonably satisfactory position in favour of an untried theoretical improvement if it is probably impossible to return to it should the theory prove false (cf., among other things, nationalization).—I am, etc.,

Burton-on-Trent. RANDLE LUNT.

Electro-convulsive Therapy

SIR,—The following method is used for giving electro-convulsive therapy at Cork Mental Hospital. The patient receives 1/100 gr. (0.65 mg.) atropine sulphate ten minutes before stimulus, followed by thiopentone sodium, 0.15–0.25 g. intravenously. The syringe is disconnected, but the needle remains intact, and through it is injected succinylcholine, 50 mg. As soon as fibrillation ceases the patient's lungs are inflated 3–4 times with oxygen, using a mask and rebreathing bag. The headpiece is then applied and the electrical stimulus is given.

We would like to record the following observation which may be of interest. If the pupil contracts immediately after the stimulus we have noticed that a convulsion very rarely occurs. Owing to the short time factor involved before the succinylcholine wears away, we now feel it safe to give another stimulus straight away, as there seems to be little danger of a delayed convulsion. We have found this sign very useful and wondered if other readers have had any similar experience.—We are, etc.,

E. THOMAS.
B. F. HONAN.

Cork.

Christmas Disease

SIR,—The correspondence which has followed publication of the article by Dr. Rosemary Biggs and colleagues on "Christmas Disease" (*Journal*, December 27, 1952, p. 1378) has raised several important questions, including that of nomenclature. Dr. A. S. Wiener's suggestion that this disease be called haemophilia II or B (*Journal*, March 7, p. 559) has merit because it focuses attention on the genetic similarity to classical haemophilia. His proposal, however, is based on the assumption that the mutant genes for classical haemophilia and Christmas disease occupy the same locus on the X chromosome—that is, they are alleles. We believe this assumption to be incorrect. There are well-defined differences, biological and chemical, between the normal plasma components which prevent haemophilia and Christmas disease. For example, the factor preventing haemophilia (AHF) is not absorbed by $BaSO_4$, and its activity diminishes during clotting. On the other hand, the "Christmas factor" is absorbed on to $BaSO_4$, and its activity increases during clotting.

It was suggested that the same allelic relationship exists between Christmas disease and classical haemophilia as exists between mild and classical haemophilia. This analogy, we believe, is unsound. The two forms of haemophilia, resulting from different degrees of reduction of the *identical* plasma protein, AHF, are due to the mutant genes h and h^m; Christmas disease, resulting from diminution of an entirely different protein, is probably due to a mutant at a different locus on the X chromosome. The facts that normal plasmas, even in males with the single X chromosome, possess both AHF and Christmas factor, that haemophilic plasma contains "Christmas factor," and that AHF is present in Christmas disease can hardly be interpreted in any other fashion. Linkage studies would be most valuable.

As for the problem of nomenclature, we suggest that haemophilia and Christmas disease be grouped with the other haemorrhagic diatheses which are characterized by absence or malfunction of a specific plasma protein required for normal clotting, and a resultant clotting defect due to impaired conversion of prothrombin to thrombin. Haemophilia is the archetype of this group of diseases. The name "haemophilia" is hallowed by tradition and deeply ingrained in the literature; we suggest that its use be limited to those haemorrhagic states due to inadequate AHF. For the other diseases meeting the above criteria we suggest the term "haemophilioid states."

The following table indicates the presently described members of this group of haemorrhagic diseases. The proposed classification has the merits of simplicity and elasticity. When the exact chemical impairment in each disease is known, more meaningful terms, neither eponymic nor arbitrary, can be applied. An elaboration of this classification, along with diagnostic criteria, will be published soon.

Disease State	*Synonyms*
Haemophilia	
Haemophilioid state A	Parahaemophilia, accelerin, or AcG deficiency
Haemophilioid state B	Hypoproconvertinaemia, spca-deficiency
Haemophilioid state C	"Christmas disease," PTC-deficiency
Haemophilioid state D	PTA-deficiency.

—We are, etc.,

JOHN B. GRAHAM.
K. M. BRINKHOUS.

Chapel Hill, N. Carolina.

Controlled Respiration and Apnoea in Anaesthesia

SIR,—Dr. Gordon M. Wyant (*Journal*, June 13, p. 1334) recommends anaesthetists not to lose sight of the fact that apnoea "is essentially an unphysiological state of affairs." Now what does Dr. Wyant mean by "unphysiological"? How, for example, would he achieve, in his sense, "physiological anaesthesia"? Surely it must be admitted that anaesthesia essentially is unphysiological, in that it involves interference with the normal mechanisms of maintaining the internal environment. It is, for example, true to say that under general anaesthesia it is impossible to produce relaxation of the abdominal muscles without some involvement of the respiration. It is under these conditions that "the lesser of the two evils" is to have ventilation of the lungs which is artificial but efficient, rather than that which is natural and impaired.

Professor E. A. Pask (*Journal*, May 9, 1048), writing on the same subject, believes that "many physiologists will be surprised to learn that positive pressure ventilations can be carried out at all without causing some disturbance in the cardiovascular system." It is not clear in this context whether he necessarily implies by the term "disturbance" a resultant reduced efficiency. We are sure he would join us in wishing to refer these physiologists to the all-important work on human subjects carried out by Cournand and his colleagues.[1] These workers showed that, given the correct intrapulmonary pressure curve, artificial inflation of the lungs did not, in fact, impair cardiac function.

We would conclude with two points: (1) It appears that the term "unphysiological" is being too loosely used. In artificial circumstances, for example, during anaesthesia, the maintenance of the internal environment to comply with cellular requirements—that is, normal physiology in Claude Bernard's sense—may imply the use of artificial methods. (2) Many in the vanguard of modern anaesthetic progress still maintain a regard amounting almost to a superstition for the authority of the—to quote Professor Pask—"old-fashioned" anaesthetist. We are not, however, prepared to believe that the virtue of being old-fashioned gives any doctrinal authority in respect to the matters under discussion.—We are, etc.,

G. JACKSON REES.
T. CECIL GRAY.

Liverpool.

REFERENCE

[1] *Amer. J. Physiol.*, 1948, **152**, 162.

The Post-operative Chest

SIR,—Mr. V. J. Downie's remarks regarding the treatment of the "post-operative chest" (*Journal*, June 20, p. 1388) cannot be allowed to pass without comment.

During the past 25 years or so, many workers have investigated this problem very carefully; if would be a great pity if their work were to be wasted because it came to be accepted that prevention and treatment based on a proper understanding of the pathology of this condition was of little or no importance. Mr. Downie suggests that a good anaesthetic technique will prevent these complications. This is certainly not the case. A bad anaesthetic technique may certainly increase the incidence of post-operative chest com-

plications, but the best technique cannot reduce it below a certain minimum level. This is because anaesthesia, if any reasonable technique is used, is not an important factor in the causation of the condition. The cause of nearly all post-operative chest complications is the gross interference with respiratory mechanics and in particular with the cough mechanism which results from certain operative procedures —notably upper abdominal incisions, hernia repair, thoracotomy, and thyroidectomy. When the operation does not involve one of these incisions post-operative chest complications (apart from hypostatic pneumonia in the old, enfeebled patient) are practically non-existent. I recently anaesthetized a patient suffering from chronic bronchitis for repair of a ventral hernia using a ventral sheath block combined with a small dose of thiopentone. Post-operatively he developed a well-marked basal segmental collapse with pyrexia and mucopurulent sputum. It is difficult to see how the anaesthetic could have caused this, but one had only to watch the patient for a few minutes to appreciate the very real difficulty he had in coughing up his sputum.

I quite agree that it is very doubtful if post-operative segmental collapse commonly results in bronchiectasis, but I do not think that this is any reason for failing to treat a condition which is usually easily diagnosed and which often responds to relatively simple measures. It is true that these cases "respond" to antibiotics in that the temperature returns to normal, and I agree that they have an important part to play in prevention and treatment. Nevertheless they often fail to have any effect on the underlying pathological condition, which is the blocked bronchus. Several years ago, as a junior resident anaesthetist, I saw a patient discharged from hospital with definite radiological signs of segmental collapse, the result of an operation about two weeks earlier, still present. She had been on routine penicillin, and there was little in the way of symptoms or general upset. I do not think that either the patient herself or the surgeon in charge realized that there had been any pulmonary complication. Quite probably her atelectasis later expanded without leaving any permanent pulmonary damage, but I think it would have been better if she could have left hospital with her lungs in the same condition as when she entered.

Prevention and treatment need not be either elaborate or expensive, and certainly should not be aggressive. Routine breathing exercises by themselves are useless and a waste of time (I do not, of course, deny that they have an important part to play in the preparation of the patient for certain operations). There is no substitute for the careful pre- and post-operative examination and individual treatment of each patient undergoing the type of operation I have mentioned. When atelectasis is diagnosed or suspected the patient must be encouraged and assisted to clear the blocked bronchus in whatever way seems best for him. If simpler methods fail bronchoscopic suction should probably be used, although it is rarely necessary.

The last word on this problem has probably not been said. The value of the routine use of bronchial antispasmodics has not, I feel, been proved. Nevertheless, using the relatively simple methods so clearly set out by Brock[1] many years ago, we can do much towards the prevention and satisfactory treatment of post-operative chest complications to the probable benefit of the patient.—I am, etc.,

Omagh, Co. Tyrone. W. S. DAVIS.

REFERENCE

[1] *Guy's Hosp. Rep.*, 1936, **86**, 191.

Possible Sequel of Treating Infants in Erect Posture

SIR,—At the follow-up clinic last week I saw two infants, both aged nearly 7 months, who had been treated for hiatus hernia by being placed in the erect posture day and night for the last four months. Both of them now have skulls somewhat flat on the top, and the circumference of one is 17¾ in. (45 cm.) and of the other 18½ in. (46.7 cm.). The skulls appear to have altered in shape, and have not the characteristics of those of other members of the families.

It is possible, I believe, that such a shape of skull may be a sequel of treatment in the erect posture. The condition is being further investigated, but I write now to ask if any other observers have found flattening of the skull resulting from such treatment.—I am, etc.,

Aberdeen. JOHN CRAIG.

Intravenous Pituitary Extract in the Control of Haemoptysis

SIR,—I feel that a word of caution should be added to the letter by Dr. N. D. J. de S. Wijesekera (*Journal*, June 20, p. 1389) on the use of intravenous pituitary extract in the control of haemoptysis. In the course of clinical investigations on the action of pituitary extract—admittedly for reasons far removed from the control of haemoptysis—I have given scores of injections by various routes and have come to regard the single-dose, intravenous injection with a respect bordering on trepidation. Dr. Wijesekera was fortunate that after the administration of 10 units no more ill effect was seen than that "the patient's face assumed a cadaverous hue except for a faint malar flush." I strongly urge that if this very potent substance is to be given intravenously by a single injection a dose of one unit (or certainly not more than two units) should be used, and this small volume of solution well diluted in saline and given very slowly, as Dr. Wijesekera in fact advises. If intramuscular injection is employed a somewhat larger dose may be permissible.

To compare the doses employed by workers 40 years ago with those in use to-day is meaningless, for standardization of pituitary extract did not become established until the late nineteen-twenties.—I am, etc.,

Oxford. J. CHASSAR MOIR.

Television Glaucoma

SIR,—Since the advent of television to Northern Ireland I believe the following is the first case of acute glaucoma which commenced while the patient was viewing television.

A lady of 80 years of age, seeing television for the first time, watched with enthusiasm the Coronation service and processions. During the late afternoon her right eye became red and painful. When seen by me the following day the eyeball was hard and congested, the cornea was hazy, and the pupil was dilated—typical acute congestive glaucoma. She was unaware of any previous eye trouble.

It is well known that when instability of intra-ocular tension exists an abnormal rise of tension may take place on remaining in a dark room or when accommodating, as on close reading for about an hour. It would thus appear that prolonged periods of television viewing, especially in a darkened room, are not without risk to the aged and to those with certain recognized eye defects.—I am, etc.,

Belfast. V. A. F. MARTIN.

Mammary Abscess

SIR,—The limitations of the antibiotics in curing mammary abscess are referred to in Mr. C. P. Mills's paper (*Journal*, June 27, p. 1427), as also are the difficulties encountered later in dealing surgically with encapsulated pus.

Early drainage would appear to be indicated by Mr. Mills except in those cases which were effectively treated with an appropriate antibiotic in the initial acute stage. Even assuming that most, if not all, the infections are staphylococcal, it must be extremely difficult to isolate the causal organism in the early inflammatory stages. Many inflammatory symptoms of mastitis disappear entirely without treatment, and pus formation is a late manifestation in any case—so much so that the bulk of the cases present themselves after they have been discharged from the maternity hospital.

My experience as a medical officer of health and former superintendent of hospitals has been that mastitis is primarily a hospital infection due to a staphylococcus which cannot be traced readily either to faulty technique or to individual members of the staff. Empirical measures, based on the assumption that the causal organism builds up in the dust and air of the wards from time to time, have been successful in reducing dramatically any outbreak. The tragedy lies in the fact that much suffering and disability occurs before these measures—which temporarily disorganize the hospital—can be taken.

It has always appeared to me as an epidemiologist that maternity hospital infections should be preventable and that

the staphylococcus—the enemy No. 1 of such hospitals—warrants urgent attention with all the resources at our command. The direct approach is undoubtedly to identify the presence and establish the source of any pathogenic strain of the organism. This, alas, is fraught with technical difficulties these days when it is no longer possible to direct operations under a unified command. In promoting the first local health authority scheme (staphylococcal investigation) for research to be approved under the National Health Service Act I had hoped to get the necessary typing done, but it appears that no laboratory in Scotland can do this. I can only suggest therefore that the work be carried out by the Medical Research Council laboratory services in conjunction with a maternity hospital where accurate control can be exercised over the investigation. I know that there is any amount of clinical material, and the resulting recommendations may well abolish a most distressing condition which is admittedly difficult to treat.—I am, etc.,

Kirkcaldy. J. W. R. HAY.

Hypnosis in Modern Medicine

SIR,—Professor Alexander Kennedy (*Journal*, June 20, p. 1377) takes me to task for stating, in *Hypnosis in Modern Medicine*, that we should "detensionize the child with hypnosis and the anxiety will fall to pieces." This statement is, of course, taken from its context. What I actually say is: "I have tried to show that tension is the root of most childish ills and I have coined the word *detensionize* to explain this reaction to hypnotic suggestion. Seemingly conflict, repression, and frustration, given the right soil, grow anxiety, which produces tension and finally a neurosis. . . . Detensionize the child with hypnosis and the anxiety will fall to pieces, allowing the physician to re-educate both child and parents. . . ."

Professor Kennedy is upset that "two articles by British contributors . . . do not fairly represent British medicine." May I remind Professor Kennedy that hypnosis has been viewed with suspicion, incredulity, aggression, and emotional bigotry for nearly 200 years by those very physicians who should have led the profession to a knowledge of the subject?—I am, etc.,

Carshalton Beeches, Surrey. GORDON AMBROSE.

Spiritual Healing

SIR,—I would be grateful for space in which to invite information from medical colleagues with knowledge of patients treated by spiritual healers. By "knowledge" I mean adequate medical case-histories with radiographs and other records before and after treatment.

My search on behalf of the Society for Psychical Research is for documented cases likely to stand up to investigation of the organic state following such "healing." The experience of others in this field would be most helpful in widening the scope of investigation and the reliability of conclusions.—I am, etc.,

45, Wimpole St., London, W.1. LOUIS ROSE.

POINTS FROM LETTERS

Dental Sepsis

Dr. T. STORDY (Surbiton) writes: I should like to make a plea for the patient whom we treat according to modern methods, and would beg the dentist, with the utmost urgency, to remember that there is a patient attached to the tooth, and most grievous general conditions are produced by anything septic in the mouth. *X*-ray films of teeth cannot be relied upon absolutely. I have carefully observed thousands of dead teeth, teeth filled in all parts of the world, teeth which have had apicectomy performed on them, or have been splinted for periodontitis and passed as being free from infection, but which on extraction showed signs of long-standing subacute inflammation. . . . We have all carried out this treatment and seen the results of our own and others' efforts, in the vast majority of cases to the patient's detriment. In this connexion I very strongly urge the teaching of more general medicine to the dental student, so that he may be able to recognize the signs of sepsis and low resistance to toxins.

Obituary

VICTOR BONNEY, M.D., M.S., F.R.C.S., F.R.C.O.G.

We record with regret the death on July 4 of Mr. Victor Bonney at the age of 80. With the late Sir Comyns Berkeley, also of the Middlesex Hospital, he did much to raise the reputation of British gynaecological surgery to its present high position.

Victor Bonney was born in Chelsea on December 17, 1872, the son of Dr. W. A. Bonney, a well-known physician and surgeon. He studied medicine at the Middlesex Hospital, graduating M.B., B.S. in 1896 and proceeding to the degrees of M.D. in 1898 and M.S. in 1899, the year in which he also became a Fellow of the Royal College of Surgeons. To complete this impressive list of degrees and diplomas he became a Member of the Royal College of Physicians in 1900 and took the B.Sc. (anatomy) of London University with first-class honours in 1904. After resident appointments Bonney won the Emden research scholarship in the Cancer Investigation Laboratories of the Middlesex Hospital. His interest in obstetrics and gynaecology was not slow to develop and as early as 1905 he was appointed obstetric tutor, becoming assistant gynaecological surgeon in 1908. When Sir Comyns Berkeley retired in 1930 he succeeded him as senior gynaecological surgeon. Bonney and Berkeley, who were both great teachers, worked together to extend and perfect Wertheim's operation for cancer of the cervix and they were the joint authors of the well-known *Textbook of Gynaecological Surgery*. When the fourth edition of this work was reviewed in this *Journal* in 1943, the author of the review wrote:

[*Lafayette, London*

"Scattered throughout the British Commonwealth of Nations there is a band of younger men whose privilege it has been to serve an apprenticeship at the Chelsea Hospital for Women, London, where they have become imbued with the Berkeley–Bonney tradition. They are the disciples of the Bonney technique and the Bonney conservatism, and to them, as to many others, Bonney is the greatest living exponent of gynaecological surgery. They remember him as an exquisite surgeon, a stimulating thinker and leader, and a rare and generous teacher."

Bonney's other contributions to the practice and literature of gynaecology were numerous and important, and he devised a number of ingenious instruments.

During the first world war he worked as a surgeon at the military branch of the Middlesex Hospital at Clacton-on-Sea. For many years he was on the staff of the Chelsea Hospital for Women, and at one time or another he held appointments at the Royal Masonic Hospital, the Miller General Hospital, Putney Hospital, and Queen Alexandra's Military Hospital. He was also visiting gynaecologist to the Postgraduate Medical School in London. On the council of the Royal College of Sur-

geons Bonney played a noteworthy part and rose to be a vice-president of the College. He was Hunterian lecturer in 1908, 1930, and 1931, Bradshaw lecturer in 1934, and Hunterian Orator in 1943. The Royal College of Obstetricians and Gynaecologists conferred on him the Honorary Fellowship of the College in 1946. During a visit to Australia he was made Honorary Fellow of the Royal Australasian College of Surgeons, and the Association of Surgeons of Great Britain and Ireland and the American Gynaecological Society in the U.S.A. paid him similar honour. For many years he was a member of the council of the Central Midwives Board, and he examined for the Conjoint Board and several universities. In 1923 he was president of the Section of Obstetrics and Gynaecology at the Annual Meeting of the B.M.A.

Victor Bonney painted and drew with great skill. Not only did he regularly exhibit his paintings at exhibitions of work by medical artists but he illustrated his own books with admirably clear drawings. When he retired he went to live on the banks of the Wye, where he could indulge in another favourite hobby, fishing.

In 1905 he married Annie, daughter of the late Dr. James Appleyard, of Longford, Tasmania.

We are indebted to Sir GORDON GORDON-TAYLOR for the following appreciation:

A friendship of exactly fifty years compels a tribute from a colleague and perhaps condones the venture of a general surgeon to appraise the work of a specialist. In 1903 Victor Bonney returned as gynaecological tutor to the medical school that cradled him, full of enthusiasm, his lectures brimful of references to Teacher's ovum and the views of Targett, Schlagenhaufer, and Bland-Sutton on ovarian tumours. It was Bland-Sutton who had directed his footsteps to the Chelsea Hospital for Women, who had turned his gaze towards pelvic surgery, and to whom he always expressed his indebtedness for anything which he himself had achieved. By 1903 he was already on the staff of "Chelsea" and forging ahead as a skilful and intrepid operator. He had already accumulated a plethora of academic degrees and diplomas, but despite the fullness of his days the attraction of a recently created B.Sc. degree in anatomy of the London University made him ready and eager to sacrifice his nights also to attain his ends. I had the immense privilege of working with Bonney for a whole year in the dead of night, when four times a week the two companions toiled through the livelong night, only ceasing at 12.45 a.m. on the other three evenings in the week. Friendships forged in such an environment last as long as life endures. Not only did this year of prodigious toil secure its academic reward, but it also revealed to Bonney that he could draw, and it would be superfluous to refer to the self-drawn illustrations with which he has always adorned his books and scientific communications. The discipline of that year also introduced him to histological methods, which he at once turned to account in his work as Emden Research Scholar in the Middlesex Cancer Laboratories and also in the elucidation of the phenomenon of the implantation of the ovum in cases of tubal gestation, which was engaging his attention. Bonney was quick to recognize that gynaecology and the maieutic art constituted a branch of surgery, and first at "Middlesex" and subsequently in most institutions those who practised the specialty were destined no longer to be "men-midwives" but surgeons with the proud prefix of "Mr." to their name. If Lawson Tait and Bland-Sutton first rescued womankind with their pelvic tumours from the inert, inept "men-midwives" who had previously "treated" their ailments, it was Victor Bonney who became the scintillating ornament of gynaecological surgery.

Bonney was made of such stuff and fibre that he would have excelled in any branch of surgery that his fancy selected. I would not dare to compare the perineal surgery of one operator with that of another, but I have seen the Wertheim operation performed by gynaecological surgeons throughout the whole world, and among these Bonney stood supreme. He knew every trick of the tool's true play, and had an inventive turn where instruments were concerned: many of the surgical gadgets in use in gynaecological and other operating theatres owe their origin to him. Victor was not content to limit his sphere of surgical activity to the pelvis and had his own views about the treatment of gall-bladder disease, and one of the last operations which he performed only a few months ago was a radical operation for cancer of the breast.

He was the first gynaecologist to secure a seat on the council of the Royal College of Surgeons of England, and served the council for twenty years, and the first of his specialty to become an Honorary Fellow of the Association of Surgeons. The lack of emphasis on surgical training in the requirements for the diplomas of the recently created College of Obstetricians and Gynaecologists aroused his strongest disapproval, and only when years later this defect was remedied would he accept the Honorary Fellowship of that College. He was the first Honorary Fellow of the Royal Australasian College of Surgeons, being admitted to the Fellowship at the same time as Lieutenant-General Sir John Goodwin, then Governor of Queensland (1928).

Victor was a man of intense kindliness, and his quaint address of endearment, though perhaps not advancing his promotion in the councils of men, nevertheless revealed the heart of gold that beat within his breast. His loyalty to colleagues was one that "passeth all understanding," and the memory still remains with me of an enthusiast who half a century ago prepared the specimens, the paraffin blocks, employed the histological stains, wrote most of the paper or book, made the drawings, while the contribution of his co-author was confined to turning the handle of the microtome. Yet he went his smiling way, nor did any rancour impair the lightness of his step. His married life, which lasted nigh on fifty years, was one of great happiness, and to the end of his life he remained the same devoted lover as he was fifty years ago in his courting days, when every morning he wrote a note to his fiancée and scampered across the hospital quadrangle from our dissecting room to catch the 3 a.m. post which existed in that far-distant period. To the writer of this tribute he was a great master surgeon and a loyal friend.

EWEN A. JACK, O.B.E., Ch.M., F.R.C.S.Ed.

Mr. Ewen A. Jack, lecturer in orthopaedic surgery at Edinburgh University and consultant orthopaedic surgeon for the South-Eastern Region of Scotland, died at his home in Edinburgh on June 28 at the early age of 44.

Ewen Alistair Jack was born on January 31, 1909, at Hartlepool, where his father was in general practice, and was educated at Fettes College. On leaving school he studied medicine at the University of Edinburgh, where he distinguished himself as an athlete, being captain of the University Rugby fifteen. While at the University he lived in Ramsay Lodge, and there must be many Ramsay men the world over who will mourn the loss of their old friend, cut off at the peak of his career.

Ewen Jack graduated M.B., Ch.B. in 1932, and after a series of house appointments in Edinburgh and Leicester became a Fellow of the Royal College of Surgeons of Edinburgh in 1935. A period of post-graduate training in London followed, and he then returned to Edinburgh as clinical tutor in surgery at the Royal Infirmary, an appointment he continued to hold till the outbreak of war in 1939, when he entered the R.A.M.C. Up till then Jack's aim had been to secure a sound general training in surgery, and it was on this that he rapidly built up experience in his chosen specialty of orthopaedics.

He had a distinguished career in the Army, serving with the British Expeditionary, Middle East, and Central Mediterranean Forces, both as an orthopaedic specialist in charge of a large orthopaedic centre in Cairo and as the officer in charge of a field surgical unit in Sicily and Italy. He was then promoted lieutenant-colonel with charge of the surgical division of a general hospital in north-west Europe, where he served till demobilization. He was appointed O.B.E. in 1944 in recognition of gallant and distinguished services in Sicily, and in the following year he was mentioned in dispatches for his services in north-west Europe. It was while serving with No. 9 General Hospital in France in 1940 that he met his wife, formerly Miss Vivien Weekes, and they were married in Cairo early in the following year.

Edinburgh was indeed fortunate that he chose to settle down in his old school after the war. He played a notable part in the formation of an orthopaedic scheme for the area and was instrumental in its success. It was typical of his drive and determination that in the midst of this exceptionally busy time he obtained the higher degree of Ch.M. in 1948. His skill and ability as a teacher and as a surgeon were known not only to the students in Edinburgh but to a far wider circle, as was evident at the joint meeting of the Orthopaedic Associations of the English-speaking World in London last year. It was characteristic of him that his interests were not confined to a limited sphere but to the advancement of orthopaedic surgery in general. He was an indefatigable worker and had an uncanny ability to strip a problem of its non-essentials, having a keen eye for the basic facts. He made several important contributions to the literature of his specialty, and his many friends will not be surprised to learn that when even his stout heart could not drive his broken body to the physical effort of attending to his patients he was still actively engaged in the preparation of another paper, which, alas, he was not to be allowed to finish.

Ewen Jack was a big man, physically and in every other way. Those who knew him well and worked with him entertained a tremendous respect for his judgment and a high regard for him as a companion. Any of his gifts would have brought a man honour, respect, and admiration, but he had an even greater gift, and that was personal courage. A few months ago he knew that his end was near, but there was never any suggestion of limiting his activities. Indeed, he worked under a terrific physical burden till three weeks before his death. Those who knew of Ewen Jack's end realized that here was a man who set a fine example of how to die nobly. He died at home within sight of the beautiful garden of which he was so proud and which he had been allowed to enjoy for such a short time. No man could have been better nursed than he was by his wife. Her courage and devotion were an inspiration to all who were privileged to be with him during his last illness. To her and to his two young children goes our deepest sympathy.—J. H. C. and W. M.

OSWALD MARRIOTT, M.D., M.R.C.P.

Dr. Oswald Marriott, well known in Hong Kong and in London, died on June 17 at the age of 79.

Oswald Marriott was born on December 30, 1873. From Dulwich College he went to Guy's Hospital to study medicine, qualifying in 1900. After resident appointments at Guy's and the Dreadnought Hospital, Greenwich, he continued his medical education in Vienna and Brussels and at the London School of Tropical Medicine. He took the M.D. of Brussels University and then graduated M.B., B.S. at London University in 1908, proceeding M.D. (tropical medicine) in the same year. Shortly before this he had gone out to Hong Kong as a member of the firm of medical practitioners which had included among its members Dr. (later Sir) Patrick Manson and Dr. (later Sir) James Cantlie. From 1905 to 1923 he served as a surgeon to the Chinese Maritime Customs. A keen member of the council and senate of Hong Kong University, he lectured there on materia medica and therapeutics. His practice was a large and busy one, for he put his work and his patients in front of everything else. All his work was run on strictly business-like lines, and every minute was accounted for. He took a great interest in the local Branch of the B.M.A. and was for a time its indefatigable secretary. He was in the R.A.M.C. for a short time towards the end of the first world war.

After Marriott returned to England in the early nineteen-twenties he built up a consulting practice in the City of London, specializing in tropical diseases. In 1923 he took the M.R.C.P. He maintained his early interest in the affairs of the B.M.A. and was a member of Council for many years, besides serving on a number of committees and as a Representative at Annual Meetings.

We are indebted to Mr. W. SAMPSON HANDLEY for the following appreciation: The passing of Oswald Marriott severs a link of friendship which dates unclouded from the dim past of 1895. At that time he was one of the ward clerks on the firm of the late Mr. Clement Lucas, to whom Sir Arbuthnot Lane was assistant surgeon and I was house-surgeon. I recall delightful visits to Marriott's home at Forest Hill, an old manor house with gardens and orchards even then embedded in a mass of small villas.

After house-surgeoncies at Guy's and the Seamen's Hospital, Greenwich, Marriott went to Hong Kong as a member of the distinguished firm to which the late Sir Patrick Manson belonged, and henceforth his interests were mainly in tropical medicine. After a long and successful career in Hong Kong he returned to England, and until a few months before his death practised as a tropical and insurance consultant in the City, the trusted adviser of many important firms with tropical interests. He leaves a widow, two sons, and a grandson to mourn his loss, and his friends the world over will share their feelings. In him modesty was allied with high competence, unswerving loyalty to his ideals and his friends, and lifelong devotion to the demands of his profession.

ARTHUR MARTIN-LEAKE, V.C. and Clasp, F.R.C.S.

Dr. ERNEST JONES writes: The following recollection illustrates one of Martin-Leake's most prominent attributes—his modesty. He was not the first University College Hospital doctor to win a V.C. in the South African war, but when we desired to honour him in the same fashion as we had his predecessor, who was given a banquet with Dr. G. V. Poore in the chair, he firmly declined. He had "only done his duty," and he abhorred any fuss being made about it. How high his conception of "only doing his duty" was he showed in the first world war by winning a V.C. again in heroic circumstances.

We record with regret the death of Mr. J. R. LEE on March 29 at the age of 79. Before his retirement he was senior honorary surgeon at the Battersea General Hospital. John Robert Lee was born in Australia on July 17, 1873, and was educated at Grenville College, Ballarat, and Melbourne University, where he graduated M.B., B.S. in 1898. During the next few years he enlarged his surgical experience, obtaining the F.R.C.S. of Edinburgh in 1906 and proceeding to the degree of M.D. in 1908. Among the appointments he held was that of surgeon to out-patients in the

Alfred Hospital, Melbourne. Lee was a captain in the Royal Australian Army Medical Corps from 1901 to 1915, and during the first world war he served in the R.A.M.C., attaining the rank of major, and being appointed O.B.E. for his services. After the war he settled in London, taking the F.R.C.S. of England in 1923. During the last war he served as a surgical specialist in the E.M.S. A paper in which he described his experiences in the reception and treatment of air-raid casualties was published in this *Journal* in 1941.

We are indebted to Mr. JOHN SOPHIAN for the following appreciation: The recent death of John Robert Lee has brought to a close a life that was lived unselfishly. He had been spared to a ripe old age, and even in his later years his zeal in his task remained largely unabated. There are several among the ranks of consultants who will remember him with deep gratitude. Not only did he help to provide them with professional opportunity, but he fostered and guided them with kindness, wisdom, and encouragement while their maturity was being attained. Particularly will he be remembered by the poor of Battersea. For he came to the rescue and identified himself with the then Anti-Vivisection Hospital (now the Battersea General Hospital) when at the lowest ebb of its fortunes. Those who had witnessed its rapid rise to prominence thereafter equally well knew that such success was due to his devoted exertions. On many an occasion have I heard the warm appreciation of the local sick for his efforts in having established a medical sanctuary in what had been an area bereft of such aid. The poverty of the locality had restricted professional help, and the hopelessness of families faced with illness was by his wisdom and planning greatly relieved. The last decade and a half, because of the intervention of the war and a reorientation of the social system, has tended to obliterate from memory these signal services of rescue and of help.

Lee was highly qualified and was an excellent surgeon in every sense of the word. When carrying the burden of the hospital on his own shoulders, obstetrics and gynaecology had to be included in his efforts—a task in which he manfully acquitted himself. But it was as a general surgeon that he chiefly showed his skill. His was no narrow specialization, and his intrepidity carried him successfully into every anatomical region. Even towards the end of his career his approach was characterized by sound judgment and his execution by good technique. However, it was as a good man that he will long be remembered by those privileged to have known him. He was always guided by high Christian principles, and he lived his life by these ideals. In one very human moment, which I vividly recall, he confided to me how he used to undertake the long and hazardous journey by car from home to hospital during the heaviest blitz singing hymns all the way. Though his career may not have been exceptional, his memory will long be cherished, and the good he effected will ever be a monument in the hearts of the many he so unselfishly assisted. His wife predeceased him by a few years. Our sympathy goes out to his only daughter.

The sudden and unexpected death from coronary thrombosis of Dr. D. H. MCDOWELL at the early age of 41 is a tragic loss to his family, his friends, and to the Three Counties Hospital at Arlesey, Bedfordshire, which he served so well. Daniel Henry McDowell was born on July 7, 1911, and received his medical education at Dublin, where he took the diplomas of L.R.C.P.&S.I. in 1935. After holding an appointment at the County Infirmary, Armagh, he was medical superintendent of a mission hospital at Kirin, in Manchuria, from 1937 to 1941, when he went to Australia. After practising in various places in the State of Victoria, he returned to Northern Ireland in 1945, and two years later he was appointed to the staff of the Three Counties Hospital. In 1948 he obtained the D.P.M. of the Irish Royal Colleges.

N. McD. writes: Dan McDowell will be remembered with real affection by all who knew him, and by none more so than the patients and staff of the Three Counties Hospital. Equipped with high ideals and a pleasant personality and with a quiet sense of humour, no one could wish for a more reliable or more agreeable colleague. He was more than fortunate in his married life, and our sympathy goes out to his widow and three children.

Medical Notes in Parliament

TRUTH IN ADVERTISING

Mr. PETER THORNEYCROFT on June 26 moved the second reading of the Merchandise Marks Bill, which had already passed the House of Lords. He said the effect of existing legislation was that if a trader elected to describe his goods he must not describe them falsely. The Bill widened the definition of trade descriptions to include misleading descriptions.

Dr. BARNET STROSS seconded an amendment for the rejection of the Bill. He said that in the "plugging" of things like deodorants and chlorophyll toothpaste the technique used was to make the young people and women frightened that they would become social outcasts and believe that their armpits and mouths were objectionable. Everyone associated with medicine knew that chlorophyll did not take away bad smells at all. He looked forward to seeing these people change the quality of their advertisements. The least critical of the people were subjected to advertisements of a most misleading type. One knew of advertisements of rejuvenation cures which no reputable newspaper would accept to-day and of so-called cures for incurable diseases. Such advertisers always selected psoriasis as a subject for advertising because they knew that it was not curable by any available means, but was always likely to appear to get better for a while.

Miss ELAINE BURTON said that in 1950 she had asked a Parliamentary Secretary if he was aware that the American public had the choice of 65 different kinds of aspirin which were advertised as various qualities. Some were pure, some were certified, some dissolved fast. One was advertised as giving quicker relief because it dissolved more speedily in water. It was found upon testing that the speed with which an aspirin dissolved in water was no indication of the speed with which it was absorbed into the system. It was also found that there was no relationship between the speed with which it was absorbed into the system and the speed with which it cured headache. If in this country we had advertisements of aspirins like those in America she presumed that the manufacturers or advertisers would be obliged to prove their case or they would be guilty under this Bill.

Mr. JAMES HUDSON drew attention to medicated wines. These things were sold to poor women on the assumption that what they needed was medicine. The quantity of nutritive matter contained in many of these beverages was negligible.

Mr. HENRY STRAUSS, replying for the Government, said that many of the matters that had been quoted by Dr. Stross were not trade descriptions and could not, in his opinion, be proved to be false.

The Bill was read a second time without a division.

MERGING OF MINISTRIES

On June 30 Mr. HARRY CROOKSHANK moved for the approval of a Draft Order to merge the Ministry of Pensions and the Ministry of National Insurance. He said that in 1921 there were 67 Ministry of Pensions hospitals. To-day there were only eight. There had been a marked decline in the use by war pensioners of the special hospital and treatment services of the Ministry of Pensions, which had been replaced by the National Health Service. The National Health Service had come into being for all classes of medical treatment, and the Ministry of National Insurance

did work for the industrially disabled similar to that done for the war disabled by the Ministry of Pensions. There was already a considerable link in case-work between the two departments.

Mr. GEORGE ISAACS hoped that the new Ministry, if it was established, would carry on the specialized services of Roehampton or Queen Mary's Hospital. There was another specialist centre at Stoke Mandeville which had been developed by the Ministry of Pensions and now was at the service of civilians. Miracles could be seen there. He asked for an assurance about continuation of the welfare services.

After further debate the proposed merger was approved by 226 to 212.

Priority for War Pensioners

A motion approving the Transfer of Functions (Ministry of Pensions) Order was moved in the House of Lords on July 2 by LORD SELKIRK. He said the organizational changes would take place gradually. The preferential position of war pensioners and existing priorities in regard to medical treatment would be preserved. War disabled would receive priority in the existing pensions hospitals and in all National Health Service hospitals. Treatment at clinics would be discussed with ex-Service organizations. Ex-Service interests would be represented in the management of pensions hospitals. There would be no changes in Queen Mary's Hospital, Roehampton, without full consultation with its governors.

After debate the House agreed to the motion.

Providing for Old Age

Mr. R. A. BUTLER on July 2 told the House of Commons that the Government had decided to set up an independent committee to review the economic and financial problems involved in providing for old age, having regard to the prospective increase in the number of the aged. He said the number of men and women over the ages of 65 and 60 was expected to rise from nearly 7 million in 1952 to nearly 10 million in 1977, a rise of more than 40%. In the same period the number between the age of 15 and these pensionable ages was expected to decline. Sir Thomas W. Phillips had agreed to serve as chairman of this committee. A first report was expected shortly from the Ministry of Labour Advisory Committee on the Employment of Older Workers.

Sewage in Rivers—While it is true that some tidal river estuaries are polluted by the discharge of sewage, Mr. Macmillan has no evidence of any danger to public health.

Extensions at Mental Hospitals.—Mr. Macleod hopes to make a special allocation available next year for extensions at suitable mental deficiency and mental hospitals. He has circulated to boards sketch plans to assist them in framing proposals.

Calcium.—One pint of milk (0.57 l.) supplies 680 mg. calcium; 1 lb. (0.45 kg.) of bread, containing added calcium carbonate, 649 mg.

Universities and Colleges

ROYAL COLLEGE OF SURGEONS OF ENGLAND

On July 2 Professor Lambert C. Rogers was re-elected and Professor Ian Aird, Professor R. Milnes Walker, and Professor C. A. Wells were elected members of the Council of the College. The result of the poll was as follows:

Elected	*Votes*
Lambert Charles Rogers, V.R.D. (Royal Infirmary, Cardiff)	1,206
Ian Aird (Postgraduate Medical School of London)	788
Robert Milnes Walker (Royal Infirmary, Bristol)	684
Charles Alexander Wells (Royal Infirmary, Liverpool)	640

In all 1,993 Fellows voted; in addition 22 votes were found to be invalid.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **June 20** (No. 24) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	25	1	10	1		19	1	12	2	3
Dysentery	557	79	171	2	1	188	23	59	56	
Encephalitis, acute	9	1	0	0		5	0	0	0	
Enteric fever:										
Typhoid	0	0	1	0		4	0	2(B)	0	3
Paratyphoid	23	1	2(B)	0		32	0		1	
Food-poisoning	998	16		1		116	7		2	
Infective enteritis or diarrhoea under 2 years				8	24				22	27
Measles*	7,580	291	371	233	210	7,307	745	332	210	246
Meningococcal infection	27	2	21	1		40	2	12	0	3
Ophthalmia neonatorum	37	3	12	1		31	5	9	0	
Pneumonia†	370	12	159	6		427	18	170	4	
Poliomyelitis, acute:										
Paralytic	44	3	4	5	2	28	0	9	4	
Non-paralytic	21	1				20	0			
Puerperal fever§	261	35	15	2		210	32	2	1	1
Scarlet fever	1,223	92	193	37	64	845	72	215	12	60
Tuberculosis:										
Respiratory			164	30				151	39	
Non-respiratory			40	5				35	5	
Whooping-cough	4,104	344	530	61	113	2,513	106	176	74	100

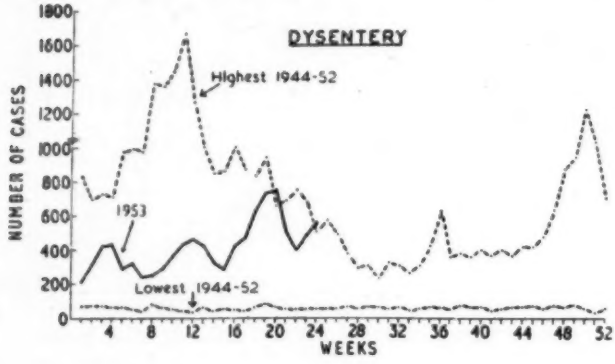
DEATHS in Great Towns	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	0	0	0		0	0	0		0	0
Dysentery	1	1				0	0		0	
Encephalitis, acute		0					0			0
Enteric fever	0	0	0			0	0		0	
Infective enteritis or diarrhoea under 2 years	6	0	0	0	1	16		2	0	1
Influenza	8	0	0	0	0	4	1		0	0
Measles		0	0		0		0		0	0
Meningococcal infection		0	0				2			
Pneumonia	148	20	19	6	4	129	21		10	3
Poliomyelitis, acute	2	0			1	2	0			0
Scarlet fever		0	0		0		0		0	0
Tuberculosis:										
Respiratory	7	1	7	3	8	91	8	10	0	6
Non-respiratory		0	3	1	0		1	3	2	2
Whooping-cough	4	0	0	0	0	3	1		0	0
Deaths 0–1 year	212	17	27	9	14	219	24	38	5	9
Deaths (excluding stillbirths)	4,447	596	529	92	127	4,587	643	523	96	130
LIVE BIRTHS	8,026	1236	937	230	362	7,973	1219	936	230	416
STILLBIRTHS	221	29	19			190	22	25		

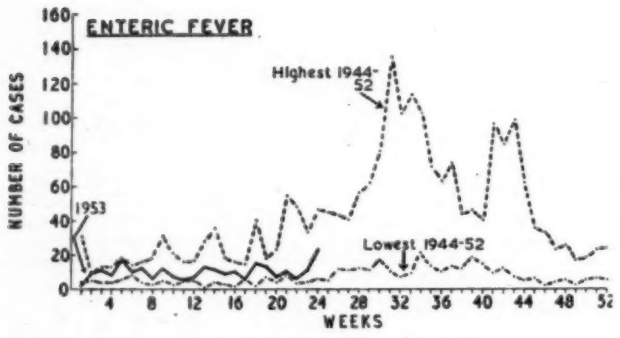
* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

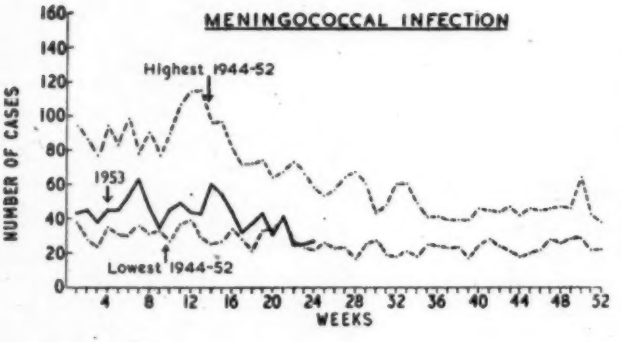
Vital Statistics

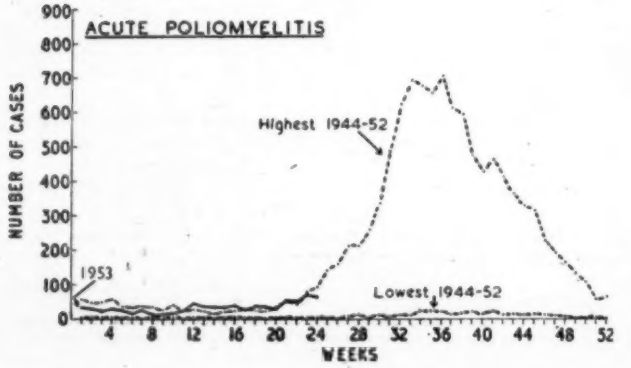
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The incidence of infectious diseases in England and Wales during the week ending June 20 increased slightly. The largest rises in notifications were 559 for whooping-cough, from 3,545 to 4,104; 168 for scarlet fever, from 1,055 to 1,223; 71 for dysentery, from 486 to 557; and 48 for measles, from 7,532 to 7,580.

The largest rises for whooping-cough were Essex 79, from 249 to 328, and Warwickshire 65, from 207 to 272. Only small fluctuations occurred in the local trends of scarlet fever. 25 cases of diphtheria were notified during the week, 8 more than in the preceding week. The rise in diphtheria was due to cases scattered throughout the country. The largest increases in the incidence of measles were Yorkshire East Riding 118, from 178 to 296; Lancashire 113, from 1,438 to 1,551; and London 84, from 207 to 291; while the largest declines were Yorkshire West Riding 139, from 843 to 704; Gloucestershire 70, from 386 to 316; and Cornwall 68, from 209 to 141.

23 cases of paratyphoid fever were notified, 18 more than in the preceding week, and this was the largest total for 36 weeks. The rise was due to sporadic cases over a wide area.

The 65 cases of acute poliomyelitis were 7 fewer for paralytic and 1 fewer for non-paralytic cases than in the preceding week. The largest returns were Kent 6, Essex 6 (West Ham C.B. 2), London 4, Middlesex 4, and Somerset 4.

The largest returns for dysentery were Lancashire 93 (Preston C.B. 27, Liverpool C.B. 21), London 79 (Islington 12), Bedfordshire 66 (Luton M.B. 59), Middlesex 50 (Edmonton M.B. 16, Willesden M.B. 12), Yorkshire West Riding 43 (Barnsley C.B. 16), Surrey 37 (Dorking and Horley R.D. 10), Leicestershire 28 (Leicester C.B. 24), and Essex 21.

Of the 998 cases of food-poisoning, 860 were notified in Lancashire. Food-poisoning was notified from 37 administrative areas of Lancashire.

Quarterly Return for Scotland

The birth rate during the first quarter of 1953 was 18.1 per 1,000 of the population and was 0.1 above the rate for the first quarter of 1952 but 0.7 below the average of the five preceding first quarters. The infant mortality rate was 34 per 1,000 registered live births; this was the lowest rate ever recorded in a first quarter, being 4 below the rate for the March quarter of 1952.

The general death rate was 13.7 per 1,000 of the population and was 0.8 below the rate for the corresponding quarter of 1952 and 1.3 below the five-years average. 219 deaths were registered from the principal epidemic diseases. These included 186 from influenza, 13 from measles, 12 from meningococcal infections, and 4 from whooping-cough. The death rate from all forms of tuberculosis was 32 per 100,000 (27 from respiratory tuberculosis); these rates were 15 and 14 respectively below those for the first quarter of 1952, and were 33 and 30 below the five-years average. Deaths from violence numbered 737, including 130 attributed to road transport, as compared with 643 and 86 in the first quarter of 1952.

Week Ending June 27

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,333, whooping-cough 4,116, diphtheria 18, measles 6,871, acute poliomyelitis 60, dysentery 676, paratyphoid fever 5, typhoid fever 4.

The Services

Major-General C. W. Greenway, C.B.E., late R.A.M.C., has been appointed Honorary Surgeon to the Queen, in succession to Major-General F. R. H. Mollan, C.B., O.B.E., M.C., late R.A.M.C., retired.

Brigadier A. E. Campbell, late R.A.M.C., has been appointed Honorary Physician to the Queen, in succession to Major-General T. Young, C.B., O.B.E., late R.A.M.C., who has retired.

Medical News

Queen's Honorary Physicians.—The following were gazetted as Honorary Physicians to the Queen for three years from July 1: Dr. G. E. Godber, deputy chief medical officer, Ministry of Health; Sir Harold Himsworth, secretary, Medical Research Council; Dr. H. L. Glyn Hughes, senior administrative medical officer, South-East Metropolitan Regional Hospital Board; Dr. J. M. Hunter, medical adviser to the General Health Services Board for Northern Ireland; Dr. E. K. Macdonald, medical officer of health and school medical officer, City of Leicester; and Dr. R. J. Peters, deputy chief medical officer, Department of Health for Scotland.

Fifth Birthday of the Health Service.—The Minister of Health and the Secretary of State for Scotland have each marked the fifth anniversary of the start of the National Health Service on July 5, 1948, by sending grateful messages to those who administer the Service. Mr. Iain Macleod speaks of the "great and remarkable tradition of this country to rely for local administration on the selfless voluntary work of thousands of men and women": "on the continuance of this work," he declares, "the National Health Service must inevitably depend." Mr. James Stuart pays a similar tribute to the "unpaid voluntary workers" who carry so much of the burden of planning and running the Service. Looking back, Mr. Stuart is able to say that the "essential services of medicine have been brought more fully within the reach of the whole population of Scotland than ever before." What do the figures tell us? In England and Wales there are now 470,000 staffed hospital beds in the N.H.S., an increase of 35,000 since the appointed day; there are 142,000 whole-time nurses and 27,000 part-time, increases respectively of 27,000 and 10,000; over 10 million dentures and 27 million pairs of spectacles have been supplied. In Scotland, the establishment of staffed beds is now 61,400; whole-time nurses number 19,000, part-time 3,400; nearly 2 million dentures and nearly 3 million pairs of spectacles have been provided.

Rockefeller Institute for Medical Research.—A New York report states that Dr. Detlev W. Bronk, the distinguished American neurophysiologist, has been nominated as director of the Rockefeller Institute for Medical Research, in succession to Dr. Herbert S. Gasser. Dr. Bronk, who was born in New York in 1897, is both an able research worker and an experienced administrator: for ten years he directed the Institute of Neurology at Pennsylvania University; during the war he was co-ordinator of research at the Air Surgeon's Office of the U.S. Army Air Forces; and after the war he was appointed chairman of the National Research Council. In 1949 Dr. Bronk was elected president of Johns Hopkins University. This experience is likely to be specially valuable, as there are to be changes in the direction of the Rockefeller Institute which will mean greater administrative responsibility for the new director.

Benefits for Occupational Diseases.—The Minister of National Insurance has appointed a committee under the chairmanship of Mr. F. W. Beney, Q.C., to review the present provisions of the Industrial Injuries Act under which benefit is paid for diseases and for personal injuries not caused by accident. The medical members of the committee are Sir Ernest Rock Carling, Dr. L. G. Norman, and Dr. Alice Stewart. The inquiry is concerned with the extent to which persons who claim they are suffering from diseases due to their employment should be eligible for the special benefits of the industrial injuries scheme. At the moment, apart from the "injury by accident" provisions, cover is given only for certain specified occupational diseases, at present numbering 40. The committee invites written evidence, which should be sent to the committee's secretary, Mr. H. B. Lewin, Ministry of National Insurance, 10, John Adam Street, London, W.C.2.

Royal Patronage for Chartered Society of Physiotherapy.—The Queen has granted her patronage to the Chartered Society of Physiotherapy. The society has been under royal patronage since the grant of its charter in 1920, when the late Queen Mary became its patron.

Professor Wilder G. Penfield, O.M., was one of the five former Rhodes Scholars to be given the honorary degree of D.C.L. at the Rhodes Centenary Celebrations at Oxford last week. Dr. Penfield is director of the Montreal Neurological Institute and professor of neurosurgery at McGill University.

Honorary Degrees at Edinburgh.—On July 3 the honorary degree of LL.D. was conferred on Dr. S. L. A. Manuwa, Inspector-General of Medical Services, Nigeria, and on Professor Charles McNeil, professor emeritus of child life and health in the University of Edinburgh.

William Marsden Travelling Professorship.—The Board of Governors of the Royal Free Hospital has awarded the 1953 William Marsden Travelling Professorship to Dr. Ernest T. D. Fletcher. He will attend the eighth International Congress for Rheumatic Diseases at Geneva, and then visit various rheumatism research centres in Italy and Spain, returning via Paris, Copenhagen, Stockholm, Malmo, and Lund. After this he will go to America, where he will visit hospitals in Canada and the United States.

Dr. H. C. Maurice Williams, medical officer of health to the county borough and port of Southampton, has been elected chairman of council of the Royal Sanitary Institute from October 1, 1953. Dr. Williams is a past president of the Society of Medical Officers of Health, and the honorary secretary of the Association of Sea and Air Port Health Authorities.

Dr. Louis Findlay, who graduated from Aberdeen University in 1936, has been appointed chief of the Health Division of the United Nations Relief and Works Agency for Palestine Refugees. Dr. Findlay's last post was that of medical consultant to the United Nations Korean Reconstruction Agency.

Dr. N. E. Waterfield has been gazetted as a Deputy Lieutenant of Surrey.

Thoracic Surgery.—Georg Thieme Verlag, Stuttgart, have commenced publication of *Thoraxchirurgie*, which will appear every two to three months and will publish papers on the pathology and surgery of pulmonary and cardiac disease. Subscription per volume of six parts is DM.60.

COMING EVENTS

British Diabetic Association.—The Annual Scientific Meeting of the British Diabetic Association will be held in the Littlewood Hall of Leeds General Infirmary on July 17 and 18. The meeting will commence with the 1953 Banting Memorial Lecture, to be given by Professor R. E. Tunbridge, whose subject will be "Socio-medical Aspects of Diabetes Mellitus." There will also be discussions on clinical experiences with new forms of insulin, and on various other topics. Accommodation may be obtained on request to the Warden of Lyddon, Virginia Road, Leeds, 2.

Postgraduate Paediatrics Symposium.—Paediatrics is the subject of the next of the monthly symposia for postgraduate students organized by the Cambridge University Medical School. The symposium will be held at Addenbrooke's Hospital, Cambridge, at 10.30 a.m. on July 18, and will comprise lecture-discussions and clinical demonstrations. Those wishing to attend the symposium are asked to notify the secretary, Cambridge University Medical School, Tennis Court Road, Cambridge, as soon as possible.

Norfolk Branch Dance.—The Norfolk Branch of the British Medical Association will hold a dinner-dance at the Samson and Hercules Ballroom, Norwich, on September 30. Invitation cards will be sent out later.

British Social Biology Council.—The Summer School of the British Social Biology Council is being held at Aix-en-Provence from August 6 to 20. The theme of the school is "Nature and Nurture." The principal speakers will be Mr. Alec Rodger and Dr. C. O. Carter. The cost of the school is £34, which includes registration, tuition, accommodation, and second-class travel. Those requiring further information should communicate as early as possible with the secretary, British Social Biology Council, Tavistock House South, Tavistock Square, London, W.C.1.

Davidson Clinic Summer School.—The Summer School of the Davidson Clinic for medical psychotherapy will be held in Edinburgh from July 29 to August 4. Further details may be obtained from the secretary of the Clinic, 58, Dalkeith Road, Edinburgh, 9.

Oesophageal Speech.—An institute on teaching and improving oesophageal speech will be held in Cleveland, Ohio, from August 10 to 16. This institute, the second to be held on voice pathology, is being sponsored by the American Cancer Society and other bodies. Surgeons and speech therapists will lecture and demonstrate the teaching of oesophageal speech, and non-speaking laryngectomized persons may attend the institute without charge. Anyone wishing for further details should write to Dr. Warren H. Gardner, 11,206, Euclid Avenue, Cleveland, 6, Ohio.

The Eighth International Congress of Rheumatic Diseases will be held in Geneva from August 24 to 28, 1953. The president is Professor E. Jarlov, of Copenhagen. Those wishing for further information are asked to communicate with Professor K. M. Walthard, Institut de Physiatrie, Hôpital Cantonal, Geneva.

The Second International Congress of Cardiology will be held in Washington, D.C., U.S.A., from September 12 to 15, 1954. Further details will be available later, but all correspondence should be sent to the secretary-general, Dr. L. W. Gorham, 44, East 23rd Street, New York 10.

NEW ISSUES

British Journal of Ophthalmology.—The next issue (Vol. 37, No. 7) will be available in a week's time. The contents include:

DEGENERATION OF THE DOG RETINA. I: STRUCTURE AND DEVELOPMENT OF THE RETINA OF THE NORMAL DOG. H. B. Parry.
AN EYE SANATORIUM: SURVEY OF ONE YEAR'S WORK. D. P. Choyce and A. G. Cross.
MODIFICATION AND DEFENCE OF THE SCLERAL IMPLANT. W. Hedley Summerskill.
THE RIDLEY INTRA-OCULAR ACRYLIC LENS. A SIMPLIFIED OPERATIVE TECHNIQUE. V. P. Patel.
FLICKER STIMULATION IN AMBLYOPIA. G. Parsons-Smith.
SECONDARY GLAUCOMA DUE TO SPONTANEOUS RUPTURE OF THE LENS CAPSULE. F. S. Hubbersty and J. S. Gourlay.
THE MEASUREMENT OF CORNEAL THICKNESS AND ITS APPLICATION TO KERATOPLASTY. A. Lister, A. S. Philps, and M. Langham.
A SPEED-OF-PERCEPTION MEASUREMENT APPARATUS. J. C. Neely.
VENOUS PRESSURE AND OCULAR TENSION. DATA CONCERNING THE DIURNAL VARIATION OF OCULAR TENSION. P. Weinstein and J. Forgács.

Issued monthly; annual subscription £4 4s., single copy 8s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Tuesday, July 14

INSTITUTE OF NEUROLOGY.—5 p.m., Dr. L. Cox (Melbourne): Disorders of Consciousness from Basal Lesions of the Brain.

Thursday, July 16

LEEDS UNIVERSITY.—At General Infirmary at Leeds, 4.15 p.m., Dr. L. B. Cox (Melbourne): Torulosis.

Friday, July 17

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, Bute Medical Buildings, St. Andrews, Fife, 11 a.m., 320th meeting. Scientific papers will be read.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Charles Tomes Lecture by Mr. G. T. Hankey: Temporo-mandibular Arthrosis.

APPOINTMENTS

DAVIES, ILID META LEWIS, M.B., B.Ch., D.Obst.R.C.O.G., Assistant Medical Officer, South-east Glamorgan Health Division.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—A. H. Millard, F.R.C.S., Surgical Registrar; M. R. Williams, F.R.C.S., Part-time Surgical Registrar; K. Till, M.B., B.Ch., Clinical Assistant to the Neurosurgical Department; N. T. Jaco, B.M., B.Ch., M.R.C.P., D.C.H., Assistant Medical Registrar; Elizabeth A. Martin, M.B., B.S., and T. J. Haywood, M.D., House-physicians; H. B. Eckstein, M.B., B.Ch., and J. A. Wilkinson, M.B., B.Ch., House-surgeons

JENKINS, DAVID HUGHES, M.S., F.R.C.S., Consultant Surgeon, United Cardiff Hospitals and Welsh Regional Hospital Board.

RICHARDS, R. D., M.B., B.Ch., F.R.C.S., Consultant Surgeon, Royal Gwent Hospital, Newport, Mon.

SLEIGH, J., M.B., Ch.B., D.P.H., Divisional Medical Health Officer, Nova Scotia Provincial Government.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—D. Finn, M.B., B.Ch., Assistant Psychiatrist at Horton Road and Coney Hill Hospitals, Gloucester; R. M. M. Hunter, M.B., Ch.B., M.R.C.P.Ed., D.P.H., D.P.M., Consultant Psychiatrist to North Gloucestershire Clinical Area; C. D. Linton, M.B., Ch.B., D.Obst.R.C.O.G., Anaesthetic Registrar, Southmead Hospital, Bristol; W. L. Walker, M.B., Ch.B., D.P.H., D.P.M., Senior Registrar in Mental Deficiency and Child Psychiatry to Bristol Clinical Area; S. Schwartz, M.B., Ch.B., F.R.C.S.Ed., Orthopaedic Registrar, Winford Orthopaedic Hospital, near Bristol; T. Galla, M.B., Ch.B., Registrar in Psychiatry to South-western Region; R. H. Ellis, M.D., M.R.C.P., Consultant Chest Physician to North Gloucestershire Clinical Area; J. M. Whelehan, L.R.C.P.&S.I., Assistant Psychiatrist, Roundway Hospital, Devizes.

UNIVERSITY COLLEGE HOSPITAL OF THE WEST INDIES.—J. B. Self, M.B., Ch.B., F.R.C.S., Surgical Registrar; J. H. M. Pinkerton, M.D., M.R.C.O.G., Senior Lecturer in Obstetrics and Gynaecology; Joyce Ford-Smith, M.B., Ch.B., D.Obst.R.C.O.G., Lecturer in Obstetrics and Gynaecology; R. A. St. C. Hoyte, M.D., C.M., D.Obst.R.C.O.G., Registrar in Obstetrics and Gynaecology.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Fluker.—On June 25, 1953, at Plymouth, to Christine, wife of Dr. J. L. Fluker, a daughter—Christine Louise.

Robinson.—On June 24, 1953, at Old Court Clinic, Ealing, London, W., to Gay (formerly Selig), wife of Dr. Keith J. Robinson, of 12, Preston Hill, Kenton, Middlesex, a son—Martin Clifford.

Shotts.—On June 28, 1953, at the West Middlesex Hospital, Isleworth, to Barbara (formerly Layman), wife of Alan Shotts, M.R.C.S., L.R.C.P., L.D.S., a son—Paul David.

Stock.—On June 27, 1953, at St. Mary's Hospital, Portsmouth, to Freda (formerly Lunt), M.B., D.C.H., wife of Dr. S. D. Stock, of 20, Magdala Road, Cosham, Hants, a daughter—Lesley Freda.

Thomas.—On June 30, 1953, at the Radcliffe Infirmary, Oxford, to Katie (formerly Walker), wife of F. Brian Thomas, F.R.C.S., Putson Manor, Hereford, a daughter.

MARRIAGES

Shirlaw—Davidson.—On July 1, 1953, at St. Andrew's Church, Waterloo, Liverpool, Herbert Anthony Douglas Shirlaw, M.B., Ch.B., Flight-Lieutenant, R.A.F., of Upholland, Lancs, to Patricia Magdalen Davidson, of Great Crosby, Lancs.

DEATHS

Cox.—On June 14, 1953, at his home, 24, Offington Drive, Worthing, Sussex, William Alfred Spencer Cox, M.D., late of Church Street, Kensington, London, W., aged 89.

Evans.—On June 20, 1953, Albert Edward Evans, C.B.E., M.B., B.S., D.P.H., Lieutenant-Colonel, R.A.M.C., retired, of 11, Weymouth Avenue, Mill Hill, London, N.W.

Feilden.—On June 13, 1953, at the Royal Surrey County Hospital, Frederick Ernest Feilden, L.M.S.S.A., late of Guernsey, Channel Islands, aged 88.

Hamond.—On June 22, 1953, at 133, Tonbridge Road, Maidstone, Kent, Philip William Hamond, M.D., aged 73.

Hayden.—On June 12, 1953, Roger Keith Hayden, M.R.C.S., L.R.C.P., of London, W. and N.W.

Holroyd.—On June 14, 1953, at Nynehead, Somerset, Gilbert Holroyd, M.B., B.Ch., Lieutenant-Colonel, I.M.S., retired, formerly of Budleigh Salterton, Devon, aged 72.

Hynes.—On June 18, 1953, Mortimer Hynes, M.B., B.Ch., of 35, Southwood Lawn Road, London, N.

Ince.—On June 21, 1953, at Woking, Surrey, Joan Katherine Somerville Ince (formerly Cave), M.B.E., M.R.C.S., L.R.C.P., of Kencot Lodge, Lechlade, Glos.

Kilner.—On June 15, 1953, at 1, Lismore, Hollington Park, St. Leonards-on-Sea, Sussex, John Newport Kilner, M.B., D.P.H., aged 79.

MacMahon.—On June 22, 1953, at 63, Milton Road, Harpenden, Herts, Charles Grant MacMahon, M.B., Ch.B.

Newell.—On June 22, 1953, Alfred George Newell, M.D., D.P.H., of 14, Dane Road, St. Leonards, Sussex, aged 80.

Sharp.—On June 19, 1953, at the Kent and Sussex Hospital, Tunbridge Wells, Kent, Leonard Whittaker Sharp, M.B., of Woodlands, Wadhurst, Sussex, aged 70.

Shircore.—On June 23, 1953, at Zomba, Nyasaland, John Owen Shircore, C.M.G., M.B., Ch.B., M.R.C.P.Ed., aged 71.

Sturdy.—On June 17, 1953, Joseph Cornelius Sturdy, L.R.C.P.&S.Ed., L.R.F.P.S., of 13, Carr Lane, Acomb, York.

Taylor.—On June 22, 1953, at Gubblecote Cross, Tring, Herts, James George Taylor, M.D., formerly of Chester, aged 78.

Tuohy.—On June 15, 1953, Joyce Tuohy (formerly Stirling), M.B., Ch.B., of Street, Somerset, late of Dunelm, Lasswade, Midlothian.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Child-bearing in the Tropics

Q.—*Are there any special dangers attending pregnancy and childbirth in a tropical climate? Would a European woman be well advised to come home, or go to a hill resort, for the birth of her baby?*

A.—A tropical climate *per se* does not create any special dangers in pregnancy, though it may be difficult to obtain proper medical attention in the Tropics. In this respect facilities vary from country to country, and it is impossible to generalize. Provided satisfactory medical attention is obtainable locally, it is not essential for the pregnant woman to return to this country for the birth of the baby. The advisability or otherwise of going to a hill resort should be decided on the relative merits of the facilities available. Other things being equal, it may be more comfortable to go to the hills if term should fall during the hot season.

Premedication for Thiopentone

Q.—*What is the safest and best premedication before thiopentone anaesthesia?*

A.—Thiopentone, like any other barbiturate, is not really an anaesthetic at all, since, so long as breathing is spontaneous and adequate, it does not abolish to any extent reflex motor responses to pain. Thiopentone is primarily a hypnotic, and it should really be used only for this purpose. In that case it provides a pleasant and rapid means of inducing sleep by intravenous injection, and when given in proper dosage interferes but little with the subsequent anaesthetic. Any premedication should have reference to the latter rather than to the small "sleep dose" of thiopentone.

Thiopentone is, however, still being used by itself as an anaesthetic—usually for short and minor procedures. In these circumstances premedication is best avoided altogether, since even the smallest additional sedative may prolong the period of recovery greatly. In general, respiratory depressants and hypnotics should be avoided before such use of thiopentone, unless the anaesthetist is prepared to manage respiratory depression and delayed recovery. If the patient is to be ambulant within a short time after thiopentone, additional sedatives, such as opiates and other barbiturates, are particularly contraindicated. The only form of premedication which is at all helpful when thiopentone alone is being used is atropine. This should never be omitted if there is any likelihood that an inhalation anaesthetic will follow the administration of thiopentone.

Pneumoconiosis without Radiological Changes

Q.—*Is a diagnosis of pneumoconiosis ever tenable in the absence of radiological changes? If so, what diagnostic criteria must be satisfied?*

A.—This question raises the difficult problem of the definition of pneumoconiosis. Pneumoconiosis is an abnormal process in the lung caused by the inhalation of dust. Theoretically it must start as soon as dust is retained in the lung and histological changes attributable to its presence develop. Such microscopic changes may be found in cases without radiological change during life. In such cases the diagnostic criteria are purely histological, and the diagnosis cannot be made during life. If the questioner implies by "pneumoconiosis" a disabling disease, then there will be radiological changes in the vast majority of cases. Occasionally coal-miners with gross respiratory disability but without radiological evidence of pneumoconiosis are found, at necropsy, to have severe focal emphysema associated with considerable fibrosis due to dust, which must have played an important part in producing the disability. Presumably the translucency of the emphysema had obscured the radiological opacities which the dust deposits might have caused in its absence. This obscuration by emphysema may be more frequent than we realize. In byssinosis there may be gross disability attributable to cotton-dust inhalation, but there are no characteristic radiological abnormalities.

A diagnosis of disabling pneumoconiosis in the absence of radiological changes must always be presumptive unless recourse is to be had to lung biopsy. It may be that in the future a specific pattern of disturbance of respiratory function characteristic of pneumoconiosis may be defined and may assist in the diagnosis, but this has not yet been done, and one can do no more than recognize the possibility that a man with respiratory disability who has had significant dust exposure may be suffering from pneumoconiosis even though there are no radiological changes.

Inheritance of Amaurotic Idiocy

Q.—*I have a patient, a first-born child aged 20 months, with amaurotic family idiocy. There is no Jewish strain on either side of the family nor any evidence of in-breeding. I should be grateful for information regarding the probable incidence of the condition in any future offspring, as the textbooks suggest the risk is considerable. Have any figures been published on actual cases?*

A.—Infantile amaurotic idiocy (Tay–Sachs disease) is due to a recessive gene. The condition is considerably commoner in Jews than in others; nevertheless it does occur with a smaller frequency amongst those who are not Jews. In this instance the parents are unfortunate in that both happen to carry the gene, and the chance that any subsequent child will be similarly affected is one in four. An excellent paper on the genetics of infantile amaurotic idiocy has been published by D. J. Home.[1]

REFERENCE

[1] *J. Genet.*, 1933, **27**, 363.

Asthma and Deep X-ray Therapy

Q.—*A woman of 60, who has suffered fairly frequent asthmatic attacks for the last 20 years, has been completely relieved of them since starting deep x-ray therapy a year ago for cancer of the breast with metastases in the lungs. What is the explanation of this?*

A.—The possibility of coincidence can certainly be dismissed, for there is quite a literature on the results of deep *x*-ray therapy of the chest and spleen in the treatment of asthma. It is generally accepted that this therapy is often beneficial in asthma—occasionally dramatically so, as in this case—but more often improvement rather than complete relief occurs, and such improvement is usually temporary. Success is commonest in the chronic long-standing or infective type of asthma, the type of asthma which responds so well to cortisone and A.C.T.H. In this connexion it is interesting that Jiménez Díaz[1] has obtained marked improvement in asthmatics from nitrogen mustard injections; in these cases there was an increased excretion of urinary ketosteroids.[2] How deep *x*-ray therapy works we do not know. Previously it was suggested that the psychological effect played a large part, but this cannot be the whole story. It may be because of its action on the reticulo-endothelial system.

REFERENCES

[1] Jiménez Díaz, C., *Rev. clin. esp.*, 1950, **38**, 122.
[2] —— *Helv. med. Acta*, 1950, Series A, **17**, 583.

Phenoxyethanol

Q.—*What are the actions and clinical uses of phenoxyethanol? Are there any special contraindications to its use?*

A.—Phenoxyethanol ("phenoxetol") is a bacteriostatic and bactericidal substance which is effective against the

pyocyaneus bacillus. It also acts on other Gram-negative organisms including *Proteus vulgaris*, although to a less extent. It has little action on the pyogenic cocci. Laboratory evidence[1] and the results of clinical trials[2] suggest that it is of considerable value. It has been used for superficial wounds, burns, and abscesses infected with *Ps. pyocyanea*, and should be applied along with an antiseptic active against Gram-positive bacteria—for example, penicillin or cetrimide.

After absorption phenoxyethanol causes drowsiness in rats, mice, and rabbits. In high doses (about 5 ml. intraperitoneally in the rat, and 16 ml. intravenously in the rabbit) it kills the animal, presumably by paralysing the respiratory centre. No ill effects have been seen in man after the application of 40 ml. of a 2.2% solution daily to a large granulating wound, and this should be regarded as the maximum safe amount. There would seem to be no other special contraindication to the use of this substance, although if it were more widely used examples of hypersensitivity reactions would probably be reported.

REFERENCES

1 Berry, H. (1944). *Lancet*, 2, 174.
2 Gough, J., Berry, H., and Still, Bess M. (1944). Ibid., 2, 176.

Use of the Title "Doctor"

Q.—*Is the use of the title "doctor" by medical practitioners not possessing the M.D. degree governed by any legislation? The minute book of an old medical club from 1826–71 designates some members as "Mr.," some as "Esq.," and some as "Dr." In 1890 it uses the term "Dr." for all members, some of whom had previously been addressed as "Mr." or "Esq."*

A.—This subject has been discussed in the medical journals on more than one occasion during the past century. In 1859 a correspondent to the *Lancet*[1] asked: "Non-graduated licentiates of the London College of Physicians being by courtesy styled 'Doctor,' may not the recently-elected licentiates of the Edinburgh College of Physicians so style themselves?"

The *British Medical Journal*[2] reported that under legal authority the College of Physicians of Ireland had assumed the right of giving the title of doctor to their fellows and licentiates (the legal authority being the Attorney-General for Ireland and the Solicitor-General for England). Again in 1862 the *Journal*[3] gave its opinion that, "as regards the prefixing of Dr. before his name, we believe that any individual can do so with impunity." Correspondence on the subject, both in the *Journal* and the *Lancet*, continued to appear sporadically until 1874, when it was summarized in a leading article in the *Journal*.[4] The difficulties of obtaining the M.D. degree by those who were otherwise qualified to practise were pointed out, and suggestions were made to remedy them. It further pointed out that "if the public choose to style every gentleman legally qualified to practise medicine or surgery by the title of Doctor, that is the public's own affair. Those only who hold the degree of M.D., obtained by examination, and not by purchase, are really entitled to it." The fact remains that the use of the title "doctor" is not controlled by any of the Medical Acts or by other legislation. It has by common practice become generally used by those duly qualified to practise medicine, whether or not in possession of a university doctorate.

The use of the title M.D. is another matter. Section 40 of the Medical Act, 1858, while not forbidding practice by the unqualified, attempts to enable the public to distinguish between qualified and unqualified practitioners. It prescribes penalties for the unlawful use of certain well-recognized titles, of which doctor of medicine is one, or any description implying that the user is registered under the Act. Even those entitled to use such a qualification may be prosecuted if they are not in the British *Medical Register*, and if such use is intended to represent that they are.[5] The Medical Act, 1950, raised from £20 to £500 the fine that may be imposed on a person wilfully and falsely holding himself out to be a registered medical practitioner.

REFERENCES

1 *Lancet*, 1859, 2, 550.
2 *British Medical Journal*, 1861, 1, 105.
3 Ibid., 1862, 1, 232.
4 Ibid., 1874, 2, 821.
5 Ibid., 1949, 1, 1144.

Comedones in Infants

Q.—*I have recently seen a breast-fed infant of 5 months who had numerous minute comedones on both cheeks. What are their cause and treatment?*

A.—It is not at all unusual for comedones to be present on the face of a very young infant, being symmetrically distributed on the nose and around the naso-labial folds. Unless they become inflamed it is probably best to leave them alone, for they will disappear without treatment in a short while. It seems likely that they have a somewhat different cause from the blackheads which are seen in adolescent acne (though the precise cause of the latter is by no means understood). The greasy skin and comedones seen in infants have been likened to a sort of miniature puberty.

Isopropyl Alcohol

Q.—*Can isopropyl alcohol be used as a substitute for methylated spirits or industrial alcohol for hospital purposes? It is readily available, not dutiable, and cheaper than ethyl alcohol.*

A.—Isopropyl alcohol is a colourless liquid which boils at 82° C. When used undiluted it is in some ways preferable to 70% ethyl alcohol as an antiseptic both for metal instruments, which tend to rust less, and for the skin, to which it is said to be less irritant. When taken by mouth it is about twice as toxic as ethyl alcohol and has an unpleasant and mildly nauseating odour and taste. Although it is not subject to duty, its use is governed by the Isopropyl Alcohol Regulations, 1927, and those who manufacture, sell, or use it must render returns to the Customs and Excise authorities.

Vitamin B and Flatulence

Q.—*Is there any known association between the oral administration of vitamin B and flatulence?*

A.—When vitamin B is taken as live yeast or as yeast tablets, some of which contain a certain amount of live yeast, fermentation may occur if the conditions in the alimentary tract are favourable, and this could produce flatulence. The vitamins of the B group could not, however, have this effect when administered in the pure state.

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